EFFECT OF COLD AND WARM COMPRESS THERAPY ON TISSUE TEMPERATURE IN HEALTHY DOGS

by

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Abstract

Objective – To measure the effect of cold and warm compress therapy on tissue temperature in healthy dogs.

Design – Controlled, blinded, crossover study

Animals – 10 healthy mixed breed dogs

Procedures – Dogs were sedated with hydromorphone 0.1 mg/kg IV and diazepam 0.25 mg/kg IV. Thermocouple needles were inserted to 0.5 cm (superficial), 1.0 cm (mid) and 1.5 cm (deep) into a shaved, lumbar, epaxial region to measure tissue temperature. Cold 2° F (-16.8° C) and warm 117°F (47°C) compresses were applied with gravity dependence for periods of 5, 10 and 20 minutes. Control data was collected under identical sedation.

Results – Mean temperature significantly decreased after 5 minutes of cold application at only the superficial depth. Application of cold for 10 and 20 minutes significantly reduced the temperature at all depths. Twenty minutes of cold application significantly decreased temperature at only the mid depth compared to 10 minutes of application. Warm compresses significantly increased temperature at all depths after 10 minutes of application. Temperatures associated with 20 minutes of warm application were not significantly different than 10 minutes of application.

Conclusions – When utilizing these methods of cold and warm compression, minimum time of application should be 10 minutes. Minimal changes occur by increasing cold application to 20 minutes and no changes occur when increasing heat application to 20 minutes. There is minimal to no change at depths ≥ 1.5 cm when using this method of heat application. Changes in

tissue temperature and side effects of application longer than 20 minutes and in the absence of *mu* agonist opioids require further evaluation.

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Chapter 1 - Therapeutic use of superficial cryotherapy

Cryotherapy is the therapeutic use of cold and is frequently used for treatment of pain, inflammation, swelling and edema associated with soft tissue trauma. Direct application of a cold object (compress) to the skin will decrease the temperature of both superficial and deeper tissues.[1-4] Lowering tissue temperature decreases tissue metabolism, edema formation, muscle spasm, pain and minimizes the inflammatory processes associated with soft tissue injury.[5-8] Lowering the metabolic rate helps protect local and surrounding tissue from enzymatic reactions associated with the injury and subsequent inflammation.[9,10] Cold reduces blood flow by increasing viscosity and by increasing vasoconstriction and reducing metabolic activity, which reduces edema formation at the site of injury.[11,12] Analgesia results from alteration in cellular metabolism and slowing of nerve conduction velocity in local sensory neurons.[13-16]

Superfical cryotherapy can be applied by numerous different methods including, ice, gel packs, ice/water/alcohol combinations, water immersion, frozen produce, and re-circulationg cooling units. Different methods of application have demonstrated various capabilities of cooling tissue. Ice and water/alcohol combinations have been shown to be superior at reducing superfical tissue temperatures, however, the results were not found at deeper tissue depths.[2,4,17,18] A 4:1 mixture ratio of water to 70% isopropyl alchohol will form a semi-solid consistance when cooled to a temperature below 0 °C making it easily conformed to body contour. The weight of ice packs has also been shown to influence degree of cooling. Ice packs that weigh at least 0.6 kg have been shown to significantly decrease skin surface temperature compared with lighter ice packs, independent of the dimensions of the ice pack.[19]

Cryotherapy is performed during the post-operative healing period in many small animal surgical patients. The use of a cold compress is very widespread and frequently justified due to the perceived beneficial results, low cost and convenient use, however, appropriate duration, frequency and overall usefulness of these therapies are largely unknown. There is no definition of an optimal frequency and duration of treatment in the scientific literature.[20,21] There are numerous human studies demonstrating the clinical effects of cold compress therapy, however, the quality of many randomized controlled trials was deemed to be quite low.[22,23] Despite the lack of large scale quality studies on the clinical effectiveness of cryotherapy, the general consensus is that repeated applications of cold for 10-30 minutes is effective at improving clinical outcome in humans.[20,21] There is currently significant debate on the appropriate recommended method of application and duration of use, as well to the actual effectiveness of cold compress therapy in clinical human patients.[20] There is very limited scientific information on this topic in dogs. In 1 study,[24] investigators found that cold compress therapy with external pneumatic compression improved signs of pain, swelling, lameness and range of motion during the first 24 hours following tibial plateau leveling osteotomy.

One area of uncertainty is the optimal temperature to which tissue should be cooled to limit secondary injury associated with soft tissue trauma. The supporting literature is limited. It is frequently assumed that greater cooling results in increased metabolic suppression and is therefore more efficacious.[2,8,10] Numerous cryotherapy studies in humans have demonstrated a wide range of temperature changes at various tissue depths, none of which have proven an optimal target temperature.[3,8-10,17] Many published studies are not controlled for method of sedation, area of cold application, method of cold application, subcutaneous tissue depth, or method of measuring depth and temperature.[21] Currently, appropriate application of

cryotherapy and heat application in dogs is largely empirical, with minimal evidence-based research, and has been extrapolated from human recommendations.

Chapter 2 - Therapeutic use of superficial heat

Thermotherapy is the therapeutic use of heat to treat disease. Heat is a widely used conservative treatment for soft tissue injury. The superficial application of heat has been proposed to aid in relief of pain, muscle spasm, promote healing, accelerate the suppurative process, cause sedation and reduce joint stiffness and muscle contracture.[25-27] It has been well established that blood flow to the skin will increase as a result of heat application.[28-30] Increased blood flow occurs by way of vasodilation and increased metabolic rate of the surrounding tissue.[28] The immediate vasodilation caused by heat application is caused by a release of substance P and calcitonin gene related peptide.[31] This immediate cause of vasodilation is only temporary. Maintenance of vasodilation is mediated by nitric oxide. Transient receptor potential cation channels that increase calcium influx into endothelial cells trigger nitric oxide release. Calcium will then activate enzyme endothelial nitric oxide synthase.[31,32]

It has been proposed that the use of heat for treatment of soft tissue injuries that have already entered the healing phase, or situations of chronic pain, that heat can be therapeutic.[33-37] One mechanism for the positive effects of heat pertains to the ability to increase blood flow and alter cellular metabolism, such that healing is further enhanced and metabolic waste products are removed at a higher rate.[26,27] Many believe that the use of supplemental heat during the acute phase of injury can cause an increase in metabolic waste products and propagate the inflammatory response in the acute time frame especially if there is impaired venous or lymphatic return.[33,34] Superficial heating over the stifle joint in human beings with paraffin resulted in elevated intra-articular temperature which as been proposed to cause further harm in patients with arthritis.[38] Alteration of pain sensation is thought to act by way of direct alteration of the stimulus and alteration of metabolic activity of neural receptors.[33,39] Increasing the

extensibility of musculotendinous units, resulting in relaxation is one example by which heat can alter the stimulus of pain.[26] In non-acute painful disorders increased blood flow may accelerate the removal of chemical stimuli thereby resulting in decreased pain levels. Increasing the temperature of a musculotendinous unit has been shown to result in lengthening, tension reduction and increased range of motion.[33,40,41] By reducing muscle rigidity, heat is believed to aid in reduction of injury associated with strenuous activity, physical therapy exercises and reduce pain associated with affected muscle groups.[33,37]

Various methods of superficial heat application include: hot packs, electric heating pads, heat lamps, paraffin, radiant light, agitated water baths, moist air baths, and dry air baths. Most thermal modalities transfer heat by way of conduction, however, some methods such as whirlpool baths can also heat by convection. Factors that influence the conduction of heat include: the thermal conductivity of the tissue, cross section area of heat path, temperature gradient in the direction of heat flow and the thickness of the conductor. The thermal conductivity of adipose tissue has been proven to be very poor relative to surrounding soft tissue.[31,42] Topical warm compresses can either be dry or moist. Moist heat application is thought to be superior and is frequently recommended for treatment of pain associated with temporomandibular joint pain.[43] Since heat will transfer at a more efficient rate when the number of free molecules available to transfer heat increases, one might infer that a liquid component would augment the heating of tissue compared to a dry counterpart. However, a study evaluating the penetration of heat from moist and dry compresses on orofacial tissue discovered that both modalities had comparable transfer of heat into tissue.[44] This study may not however, have taken into account evaporative heat loss from the moist compress that was not capable of maintaining a constant temperature. Had this been controlled for, the moist compress may have demonstrated

superior capability of heating tissue. A study that did use a moist heating source that was capable of maintaining a constant temperature demonstrated that change in skin temperature did not vary significantly between the use of a moist or dry heating apparatus, however, the moist heat caused significantly greater blood flow to the local area compared to dry heat.[31]

Although commonly recommended for treatment of long term injuries there are minimal studies to support the benefits of its use.[45] A meta-analysis evaluating use of heat for treatment of lower back pain in human beings found only moderate evidence supporting its use in a small number of trials.[46] Heat wraps that that were shown to have positive effects were only demonstrated in back pain that lasted three months or less. Patients with more chronic back pain did not experience the same positive results. In one study the addition of exercise to superficial heat application was shown to further reduce pain and improve function. This analysis cited a lack of quality controlled trials to demonstrate support of its use.[46] Application of superficial heat for treatment of soft tissue injury or chronic pain in dogs is largely empirical, with no evidence-based research.

Chapter 3 - Experimental Study

Purpose

The purpose of the study reported here was to accurately establish the effect of a commonly utilized method of cold and warm compress therapy on tissue temperature at varying depths in healthy dogs, and to establish recommendations on appropriate duration of application. We hypothesized that change in tissue temperature would be directly proportional to duration of cold or warm compress application.

Materials and methods

Animals - Ten healthy, purpose bred, mixed breed dogs were used for the study. The project was approved by the Kansas State University Animal Care and Use Committee prior to implementation of the study.

Data Collection - A 10 cm by 20 cm area was shaved on the dorsal midline lumbar region of each dog. Ultrasound was used to measure the distance from the skin surface to the deep border of the subcutaneous tissue in each dog. Each dog received hydromorphone (0.1mg/kg IV [0.045 mg/lb]) and diazepam (0.25 mg/kg IV [0.11 mg/lb]) 10 minutes prior to each data collection period. Dogs were restrained in ventral recumbency on a soft padded surface. Three 24 gauge 1.5 inch, type T thermocouple needles coupled with a thermometer were inserted into the shaved epaxial region immediately left and adjacent to midline. The needle temperature sensors were located in the distal 1mm of each needle. One needle each was inserted to a depth of 0.5 cm (superficial), 1.0 cm (mid) and 1.5 cm (deep) beneath the surface of the skin, immediately off of (left) dorsal midline. A plastic sleeve was placed over each needle (Figure 3.0.1). This allowed maintenance of accurate needle depth and avoidance of contact between the

needle and compress. Each needle remained in place for the duration of the data collection period. Rectal temperature was obtained at the beginning and end of each data collection period. Two minutes after needle insertion baseline temperatures were recorded for each depth.

Cold compresses consisted of a 16 cm x 8.5 cm x 3.5 cm commercial grade frozen gel pack cooled to 2°F (-16.8°C). The weight of each compress was 0.64 kg. Cold compresses were modified to allow passage of thermocouple needles through the center (Figure 3.0.2, 3.03). A single layer 140 cotton muslin surgical towel served as a barrier between the cold compress and skin. The towel had a similar modification to allow passage of the thermocouple needles. Dogs underwent application of cold compresses for periods of 5, 10 and 20 minutes each in a random order. Each compress was held in position by gravity, without external compression.

Warm compresses consisted of a 16 cm x 8.5 cm x 3.5 cm commercial gel pack warmed to 117°F (47°C). The weight of each compress was 0.64 kg. Warm compresses were modified to allow passage of thermocouple needles through the center (Figure 3.0.2, 3.03). No protective barrier was used between the compress and skin surface. Dogs underwent application of warm compresses for periods of 5, 10 and 20 minutes each in a random order. Each compress was held in position by gravity, without external compression

Temperature readings were recorded every minute for 10 minutes past removal of the compress, then every 5 minutes until the temperature returned to within 2% of the baseline value or until 80 minutes had elapsed. The cord adapter of each needle was color coordinated so that the individual recording temperature values was not aware which color corresponded to a given needle depth. Each dog also underwent a control data collection period, where tissue temperature was recorded as previously described, following administration of hydromorphone (0.1mg/kg IV [0.045 mg/lb]) and diazepam (0.25 mg/kg IV [0.11 mg/lb]), and no compress was

applied to the skin. There was a minimum of 48 hours between data collection periods for each dog. Each thermocouple needle was cold sterilized prior to each use.

Statistical analysis – The largest mean temperature decrease recorded at each tissue level was compared between treatment groups by repeated measures ANOVA with Newman-Keuls multiple comparison post-hoc. The largest temperature decrease at each tissue level was compared within treatment groups, between time periods by repeated measures ANOVA with Newman-Keuls multiple comparison post-hoc. Results were considered significant if $p < 0.05$.

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Results

Cold compress experiment

Ten healthy mixed breed dogs were included in the study. All dogs in the study were 1 year of age. There were 7 sexually intact females and 3 sexually intact males. Mean body weight at the time of the study was 11.0 kg (range, 8.4 to 17.0 kg). All dogs in the study had a body condition score of 3/5. The mean depth from the skin surface to deep border of the subcutaneous layer was 0.43 cm (range, 0.3 cm to 0.6 cm). No dog had a period of distress, and all dogs required minimal to no physical restraint during data collection. No dog experienced an adverse reaction at the cold compress or the needle insertion sites. The set ambient room temperature was 70°F (21.1°C) for the entire duration of the study. Rectal temperatures prior to and immediately following data collection periods did not differ significantly between control and experimental groups.

Mean reduction in temperature at the superficial depth, was 1.52°, 3.19°, 6.91° and 8.24°C for 0, 5, 10 and 20 minutes of cold application, respectively. The mean reduction in

temperature at the mid depth was 1.46°, 2.29°, 4.73° and 6.45°C for 0, 5, 10 and 20 minutes of cold application, respectively. Mean reduction in temperature at the deep depth, was 1.98°, 1.75°, 3.91° and 4.69°C for 0, 5, 10 and 20 minutes of cold application, respectively (Table 3.1, Figure 3.0.4).

Temperature for the superficial depth was significantly decreased after 5 minutes of application compared to control. There was no difference in temperature change at the mid and deep tissue depths following 5 minutes of application compared to control. Temperature at all tissue depths significantly decreased compared to control following 10 and 20 minutes of application. Temperatures for the 10 and 20-minute application periods lowered significantly more for superficial, mid and deep depths than for the 5-minute application period. There was no difference in temperature change at the superficial and deep tissue depth when comparing 10 and 20 minutes of application. The temperature decrease after 20 minutes of application was significantly lower at the middle tissue depth compared to 10 minutes of application. Superficial tissue re-warmed at a quicker rate than deeper tissue following removal of the cold compress (Figure 3.0.8).

Warm compress experiment

Ten healthy mixed breed dogs were included in the study. All dogs in the study were 1 year of age. There were 7 sexually intact females and 3 sexually intact males. Mean body weight at the time of the study was 11.0 kg (range, 8.4 to 17.0 kg). All dogs in the study had a body condition score of 3/5. The mean depth from the skin surface to deep border of the subcutaneous layer was 0.43 cm (range, 0.3 cm to 0.6 cm). No dog had a period of distress, and all dogs required minimal to no physical restraint during data collection. No dog experienced an adverse reaction at the warm compress or the needle insertion sites. The set ambient room temperature

was 70°F (21.1°C) for the entire duration of the study. Rectal temperatures prior to and immediately following data collection periods did not differ significantly between control and experimental groups.

Mean increase in temperature at the superficial depth, was -1.52°, 3.08°, 4.14°, and 4.56°C for 0, 5, 10 and 20 minutes of warm application, respectively. Mean increase in temperature at the mid depth, was -1.46°, 0.8°, 2.2°, and 2.03°C for 0, 5, 10 and 20 minutes of warm application, respectively. Mean increase in temperature at the deep depth, was -1.98°, -0.48°, 0.58°, and -0.02°C for 0, 5, 10 and 20 minutes of warm application, respectively (Table 3.2, Figure 3.0.5).

Temperature for the superficial and mid depth was significantly increased after 5 minutes of warm application compared to control. There was no difference in temperature change at the deep depth following 5 minutes of application compared to control. Temperature at all depths significantly increased following 10 minutes of application compared to control and 5 minutes of application. There was no difference in temperature change at the superficial and mid depth when comparing 10 and 20 minutes of application. The temperature of the deep depth was significantly cooler after 20 minutes of application compared to 10 minutes of application (Figure 3.11).

The warm compress underwent a cooling rate of 0.35°F (0.19°C) per minute with a total decrease in temperature of 7°F (3.8°C) at the end of 20 minutes.

Conclusion

Cold compress

The results of this study show that application of a frozen gel pack for 10 to 20 minutes will significantly reduce the temperature of tissue in the lumbar region at 0.5, 1.0 and 1.5 cm depths in medium sized dogs of ideal body condition following administration of opioid sedation without causing negative secondary effects. Previous studies in humans demonstrated that superficial tissue underwent the largest decrease in temperature as was found in this study. Many studies record the most superficial data as the skin surface.[1,2,4,17] Our most superficial level was 0.5cm beneath the surface of the skin, which is one reason that superficial temperatures in previous studies were lower then what was found in this study. The temperature change at deeper levels in our study was comparable to temperature change in deeper tissue levels in human studies.[3,17,47]

In this study there was a rapid cooling of the superficial tissue followed by a more gradual cooling of the deeper tissues. The second law of thermodynamics mandates that heat is always transferred from an area of higher temperature to an area of lower temperature. The method in which tissue is cooled by cold compress therapy is not by transfer of cold into tissue, rather heat from the tissue is conducted into the cooling apparatus. Since deeper tissues are not in contact with the cooling apparatus they cool by transferring heat to the cooler, superficial layers of tissue. Superficial tissue can act as an insulator to the deeper tissue. As the thickness of tissue increases, so does the time needed for heat to be transferred through it. In addition to tissue thickness; contact area, difference in starting temperature as well as the thermal conductivity of tissue, influence the transfer of heat.[2] The thermal conductivity of adipose tissue (0.19W·[m·°C^{-1}] is low when compared to that of other tissue such as skin (0.96 W·[m·°C^{-1}].[3] The time required

for heat to travel through adipose tissue is greater than other tissues, making it a more effective insulator compared to surrounding tissues. The effect of subcutaneous thickness on effect of muscular tissue change has been demonstrated in several studies.[3,48] One study concluded that a 20 minute treatment produced predictable temperature changes in patients with skin-fold thickness less than 20mm, however, when skin-fold thickness is increased to between 20 to 30mm, and between 30 to 40mm, the time to achieve the same degree of cooling doubles and triples respectively.[3]

This study demonstrated a significant reduction in temperature at the measured depths after 10 minutes of frozen gel compress application however; there was a significant further decrease in temperature only at the middle tissue depth when application was continued to 20 minutes. This finding did not agree with our hypothesis of a direct relationship between time of application and decrease in tissue temperature. For tissue to become cooler, the heat loss must exceed production and heat gain. Additionally, transfer of heat can only occur when a temperature gradient exists. During the initial phases of application the very large temperature difference between the compress and superficial tissue results in relative rapid tissue cooling as was demonstrated following 5 minutes of application at only the most superficial level. Fourier's law of heat conduction ($q=kA\cdot\Delta T/L$) states that the transfer rate of heat is dependent on the thermal conductivity of material or tissue, the cross sectional area of heat path, the temperature gradient in the direction of flow and the thickness of the conductor. Insulating effects increase as distance away from the compress increases. Although not as rapid, the deeper tissue eventually cools, as heat is lost to the more superficial tissue. As tissue layers continue to cool, the temperature gradients begin to decrease, slowing the rate of cooling. This is likely one component as to why there was not a significant change in temperature between 10 and 20

minutes of application at the superficial and deep levels. At the most superficial level in this study, the gradients of heat loss and heat gain narrowed quickly because of the proximity to the cooling apparatus. At 10 minutes the superficial tissue level reached a state of relative equilibrium and did not undergo a significant change with further cold application. Similarly the temperature gradients surrounding the deep layer decreased, however the relative large distance between the compress and the deep tissue depth is likely the main contributor of a lack of further temperature change after 20 minutes of application. Increasing application time from 10 to 20 minutes was not sufficient to overcome the insulating effect for the tissue between the compress and the deep tissue depth to create a significant temperature change. Significant cooling at the deep level may have continued with a longer application period. An additional component for the slower rate of cooling at the deeper tissue level may be attributed to higher level of heat production at this level. There was a significant decrease in temperature at the mid level between 10 and 20 minutes of application. To undergo continued significant cooling from the 10-20 minute time period, the mid depth had to have undergone greater heat loss than heat gain. The mid tissue level had not yet reached a state of relative equilibrium at 10 minutes and was not as insulated as the deep depth, making it capable of significant cooling during the 10-20 minute time period.

In our study the more superficial tissue underwent a rapid re-warming while the deeper tissue temperature continued to decrease in temperature and then rose more gradually, following removal of the cold compress. This is a similar finding demonstrated in previous studies.[1,49] This pattern of re-warming can be explained by several factors including removal of the source of cold on the skin, exposure of room temperature to skin, and flow of heat from the warmer deeper tissue to the cooler superficial tissue.[1,4,49] This finding suggests that at least one

of the sources of re-warming for the superficial tissue is heat exchange from the deeper tissue. Regions closer to the skin surface still have a large temperature gradient relative to deeper tissue regions. Warming of the more superficial tissue from heat transfer from deeper tissue is likely part of the explanation as to why there may be a brief period of continued cooling of deeper tissue and warming of superficial tissue after removal of the cooling device.

Despite the long-standing acceptance of its use for surgical patients, there still remains a large degree of variance in cryotherapy recommendations, in part because many studies have failed to control for numerous variables as well as questionable evidence on its ability to improve return to function following soft tissue injury.[20-22,50] In this study we evaluated the effect of temperature change of tissue, when using a common method of cryotherapy on a uniform group of dogs with similar subcutaneous tissue depths. We controlled for effect of sedation and standardized our method of temperature measurement, cold application and tissue depth measurement. We elected to place a barrier between the cold compress and the skin surface, as this is a commonly performed in a clinical setting to prevent skin burns and nerve damage during cold compression.[5,20] A physical barrier will affect the rate of cooling, however, to mimic the most common clinical application, we standardized a single layer cotton muslin towel as a barrier between the compress and skin surface.[51] We elected not to evaluate temperature change without clipping hair at the site, as the most frequent use of cold compress therapy is over a surgical site with recently clipped hair. Had we performed this study on a non-clipped region, this would likely have resulted in a reduced rate of heat conduction. We selected 2°F (-16.8°C) as the temperature for the compress to simulate a temperature that is commonly achievable with the use of a standard household freezer.

External compression on a cold compress has been shown to result in cooler tissue temperatures compared to gravity dependence.[47] We elected to use gravity dependence due to the inherent difficulty in standardizing a pressure with this method of cold compress for use in a clinical setting. The compresses used in this study were modified to allow passage of thermocouple needles. This insured desired tissue depth was maintained accurately throughout data collection by allowing needles to be inserted perpendicular to the skin surface as well as avoid artifactual temperature changes from contact with the compress.

This experiment did not have a true skin temperature measurement. It is likely that the skin surface temperatures were significantly cooler than the most superficial depth measured in this study. In one study, analgesia occurred when skin temperature reached 13.7°C and diminished when skin warmed to 15.6°C.[7] The use of a temperature probe on the skin surface may have provided useful data on the effect of this method of cryotherapy at providing analgesia. Additionally, lack of data on skin surface temperature with and without a barrier between compress and skin surface fails to determine if this model of cold compression could produce adverse effects if no barrier is used. Prolonged application of cryotherapy can result in severe complications such as nerve injury, frostbite, reperfusion injury and compartment syndrome.[52-55] There are discrepancies regarding the temperature at which skin will undergo frostbite ranging from -10.6°C to 2.2°C.[51,56,57] Peripheral nerve injury can also occur following use of cryotherapy.[15] Nerves can tolerate cooling to 10°C; functional and structural changes can occur when cooled to below 7°C.[55,58] Type and duration of cryotherapy should take into account specific patient contraindications such as underlying neuropathy, metabolic disease and those treated with long-acting nerve blocks.[53] The experiment reported here did not measure the

change in skin temperature and is unable to comment on nerve impairment or margin of safety regarding risk of frostbite.

In a previous study, superficial and deep tissue layer temperatures were measured after cold gel application in anesthetized dogs.[1] The results showed a similar rapid cooling of superficial tissues with a delayed and diminished cooling effect in deeper tissues. Re-warming periods were also longer in deeper tissue compared to superficial tissue. This study had a similar temperature change for muscular tissue after 20 minutes of cold gel pack application, however, the previous study achieved cooler subcutaneous temperatures.[1] Cold compresses are not commonly applied to anesthetized dogs, so we elected to control for sedation in our study. This previous study failed to take into account the effects of general anesthesia on tissue temperature. Induction of hypothermia is a well-recognized side effect of anesthesia. A decrease in sympathetic tone causes generalized vasodilation allowing significant heat loss from the skin surface by radiation.[59]

One of the limitations of this study was the evaluation of only one method of cold compression. We selected the commercial gel pack, as it was observed to be the most commonly used method of cold compression in our hospital. Other common methods of applying cryotherapy include various sizes and shapes of ice, frozen produce, ice/water/alcohol combinations and personal recirculating cooling units.[4,17,24] In addition to conduction, some heat may transfer by way of different methods when using other forms of cryotherapy. Melting of ice creates a wet interface on the skin allowing for heat loss through evaporation. The fact that ice goes through a change of state as it melts also allows it to absorb more heat than a cooling modality that does not undergo a change in state such as a gel pack.[2] Ice therapy has been shown to decrease the temperature of skin significantly more than gel packs for application times of 30

minutes, however, at deeper tissue (> 1 cm) the differences are insignificant.[2] Our study did not have a true skin temperature measurement. It is likely that the skin surface temperatures were significantly cooler than the most superficial depth measured in this study. We elected to modify the compresses in this study to allow for maintenance of accurate depth measurements, and avoidance of artifactual influence of cold. This necessitated that the area immediately adjacent to the needle insertion sites was not covered by the compress. Had we been able to avoid this modification the actual temperature changes may have been lower than the recorded values.

An additional limitation was the influence of sedation on tissue temperature. Administration of hydromorphone to dogs has been shown to decrease body temperature.[60,61] Specific opioid receptors are thought to induce different thermic responses. *Mu* agonist opioids such as hydromorphone, have been shown to have a thermoregulatory response that results in hypothermia in the dog.[60,61] The results of this study are supportive of a hypothermic response at the measured tissue depths. The use of *mu* agonists has a strong association with hypothermia in dogs, however, such opioids are frequently used during the same time period that cold compress therapy would be applied in small animal surgical patients, thus this model does resemble a typical clinical scenario. Diazepam is not a frequently used drug in most small animal post-operative patients. The specific influence on tissue temperature in our population of dogs is unknown. The use of muscle relaxants in human heat stroke patients have shown inconsistent results and are not routinely recommended to increase the rate of cooling.[62]

This study did not evaluate effectiveness of cold compression at improving clinical outcome, nor did it evaluate whether the tissue temperatures achieved with this model were optimal for treatment of soft tissue injury. This study can serve as a basis for future studies involving the use of cryotherapy in small animal patients. One additional direction would be to

evaluate cryotherapy of various anatomical sites and on dogs of different body condition score. Varying thickness of adipose tissue has been shown to affect the time required to cool deeper muscular tissue.[3] Additionally, evaluating temperature change following repeated application of cold could be performed.

Analysis of the results of the study reported here suggest that, using this model of cold compression on the epaxial region in dogs of an ideal body condition score, minimum time of application should be 10 minutes. When utilizing this method of cold compress therapy, there is no significant change in temperature at the superficial and deep level by increasing time of application from 10 to 20 minutes. Changes in tissue temperature and side effects of application longer than 20 minutes require further evaluation. This model appears to be a safe method of cold application in dogs.

Warm compress

The results of this study show that application of a gel compress heated to 117°F (47°C) for a period of 10 minutes, will significantly increase tissue temperature of the lumbar region at 0.5, 1.0 and 1.5 cm depths in medium sized dogs of ideal body condition following administration of opioid sedation without causing negative secondary effects. Increasing the duration of application of time from 10 to 20 minutes will not result in warmer tissue temperatures. This method of heat application results in minimal to no temperature change at tissue depths ≥ 1.5 cm.

In this study significant changes in temperature were observed at the two more superficial depths, with much less dramatic changes at the deepest measured depth. This is a similar finding that has been demonstrated in human studies evaluating effects of superficial heat application.[31,42,63,64] Subcutaneous tissue depth as been shown to significantly impair heat

transfer from modalities that are applied for periods of 10-20 minutes.[31,42] Additionally the insulating effects of subcutaneous tissue in obese people can result in accumulation of heat in the skin causing potentially dangerous increases in skin temperature.[31,42] The rate of temperature change of the superficial and mid depth decreased following 10 minutes of application. This decrease in rate of temperature change was likely a result of narrowing temperature gradients between the compress and skin surface as well as between tissue layers. Following approximately 10 minutes of application the compress had cooled to a point at which conduction of heat proceeded at a slower rate. Overall, the deep tissue level experienced minimal to no increase in temperature relative to the more superficial tissue layers. This finding again, is likely influenced by the relative narrow temperature gradients that existed in this model of heat application. Additionally, the increased distance from the source of heat and the deepest tissue depth resulted in a slower rate of heat conduction.

Similar to cryotherapy, superficial heat is widely used with significant variance on recommended method, frequency and duration of use. Additionally evidence based studies are few in number, of which only questionable therapeutic benefits have been demonstrated. In this study we evaluated the effect of temperature change associated with a common method of superficial heat application in a uniform group of dogs with similar subcutaneous tissue thickness. We controlled for effect of sedation, and accurately standardized method of temperature measurement; tissue depth and warm compress application.

Elevation of temperature with in a cell increases the motion of intracellular molecules. Increased molecular motion accelerates the rate of chemical reactions and can alter the metabolic process. Typical activation energy for many metabolic processes is relatively low (3-20 kcal/mole).[65] Short duration or low level of heat exposure results in a temporary unbalance

in metabolism and creates reversible cellular change. Longer periods of heat exposure or high intensity heat can cause irreversible changes. In *vitro* and *in vivo* studies have shown that protein denaturation is the most likely effect that causes permanent irreversible damage and cell death. Protein denaturation occurs at higher activation energies (100-200 kcal/mole) than metabolism alteration, and is dependant on time as well as temperature.[65] Alteration of genetic material has been proposed as a possible outcome of heat application. Minimal evidence exists that heat can cause damage to genetic material leading to carcinogenesis. This has only been shown in vitro in which heat induced S-phase aberrations. Mice have been exposed to heat, which showed no evidence of tumor formation, however, due to the low number of animals is the study it was determined that there were insufficient numbers to conclude that heat does not induce carcinogenesis. There are sporadic reports of the use of heat prior to administration of radiation or other tumor promoters, enhancing the incidence of tumor formation compared to the use of a tumor promoter alone. The mechanism of these results are unknown, however, it is thought to be related to the inhibition of DNA repair. In some studies when hyperthermia treatments were administered at the same time as a tumor promoter, it was found that tumorigenesis was significantly repressed.

The effect of heat on tissue can vary between species as well as within a given species.[66] Specific conditions that can increase the likelihood of thermal injury to skin include, obesity, diabetes, impaired circulation and reduced skin thickness.[31] When determining the amount of heat that is acceptable to apply to a given tissue both temperature and time are important factors. To mimic a typical clinical scenario, we held the compress to our own skin at varying temperatures to establish what felt acceptably warm without eliciting a painful response. This is a subjective method of establishing a safe temperature. The threshold for pain is different for

every person. Exposure to 46°C for 0.1 min has been shown to elicit a pain response in humans without causing detectable injury.[65] This is one degree cooler than the temperature of the compress used in this study. It has been stressed by numerous studies examining thresholds for thermal damage that a cumulative thermal dose is the most significant determinant factor in thermal damage.[65-67] The Cumulative Equivalent Minutes at 43°C (CEM_{43}) is the accepted measure for thermal dose assessment correlating with thermal damage.[67] $CEM_{43} = \Delta t R^{(43-T)}$, with Δt being length of exposure in minutes, T is the average temperature in degrees Celsius during the time interval, and R is a constant equal to 0.25 for $T < 43°C$ and 0.4 for $T > 43°C$.[67] The value 43°C has been extensively used as it has been shown that tissue damage from thermal exposure as shown on plotted curves, changes slope between 43-43.5°C for most mammalian tissues. This equation allows for a normalization of time-temperature data to determine a defined endpoint.[65] As an example if a given tissue experiences irreversible damage following 90 minutes of exposure at 43°C, then the same level of damage would be expected after 45 minutes at 44°C. When exposure drops to below 43°C the rate of damage decreases by a factor of 4. At a temperature of 42°C the same tissue would have to be exposed for 360 minutes to achieve the same level of damage.

The most sensitive organs to thermal damage are the testes and brain with damage seen at < 20 minutes CEM_{43}.[65] Bowel, cornea, retina, skin and prostate are tissues that are moderately sensitive to thermal injury. Fat, muscle, peripheral nerves, the anterior chamber of the eye, choroid, ciliary body and lens are tissues that have a relatively high threshold for thermal damage.[65] The temperature of the compress used in this study was within a safe temperature range demonstrated by previous studies evaluating thermal damage to skin and muscle.[66] A thermal threshold study showed no burns on human skin at a CEM_{43} of 240 minutes. The lowest

thermal exposure reported to cause significant injury in humans was following maintenance of skin temperature at 44°C for 200 minutes.[65] In this study we did not measure skin surface temperature, however, the highest possible CEM_{43} applied to the skin in this study for 5, 10 and 20 minutes are 56.6, 80 and 85.7 minutes, respectively. These CEM_{43} durations have been shown to be very unlikely to result in clinically significant thermal injury.[65,66]

One major limitation of this study was the effects of our method of sedation on tissue temperature. It has been well established that the *mu* agonist opioid hydromorphone, can result in a hypothermic response in the dog[60], as was well demonstrated by the temperature changes in the control group of this study. Superficial heat is typically used to treat chronic injury in patients that are not concurrently receiving injectable opioid medications. It is likely that we may have achieved warmer tissue temperatures if the tissues had not had to overcome the hypothermic effects of the hydromorphone. The specific effect of diazepam on tissue temperature in this population of dogs is unknown. An additional limitation of this study was the rate of cooling of the warm compress. A different warming pattern may have been observed had we used a heating method that was capable of maintaining a constant temperature, however, we elected to use a method that is commonly used in clinical practice. A modification of the compress was made to allow for maintenance of accurate tissue depth measurements, and to avoid tissue temperature artifact created by the influence of the warm compress. Due to this modification the area of skin immediately adjacent to the thermocouple needle insertion sites was not covered by the compress. Different changes in temperature may have been observed had we not made this modification.

This study did not evaluate whether the tissue temperatures achieved with this model were optimal for treatment of injury or pain relief. This study can serve, as a basis for

future models evaluating the use of therapeutic heat is small animal patients. Future studies may involve evaluating various methods of heat application as well as the effects of body areas of differing subcutaneous tissue depths and dogs of different body condition score. Additionally, evaluating effects on outcome in small animal patients with soft tissue injury or chronic pain.

Analysis of the results on the study reported here suggest that, using this model of warm compression on the epaxial region in dogs of an ideal body condition score, minimum time of application should be 10 minutes. There is no significant change in temperature by increasing time of application from 10 to 20 minutes. There are minimal to no changes in temperature at tissue depths $\geq$ 1.5 cm. Changes in tissue temperature and side effects of application longer than 20 minutes and in the absence of a *mu* agonist opioid require further evaluation. This model appears to be a safe method of heat application in dogs.

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Figure 3.0.1 Photograph of 24 gauge thermocouple needles.

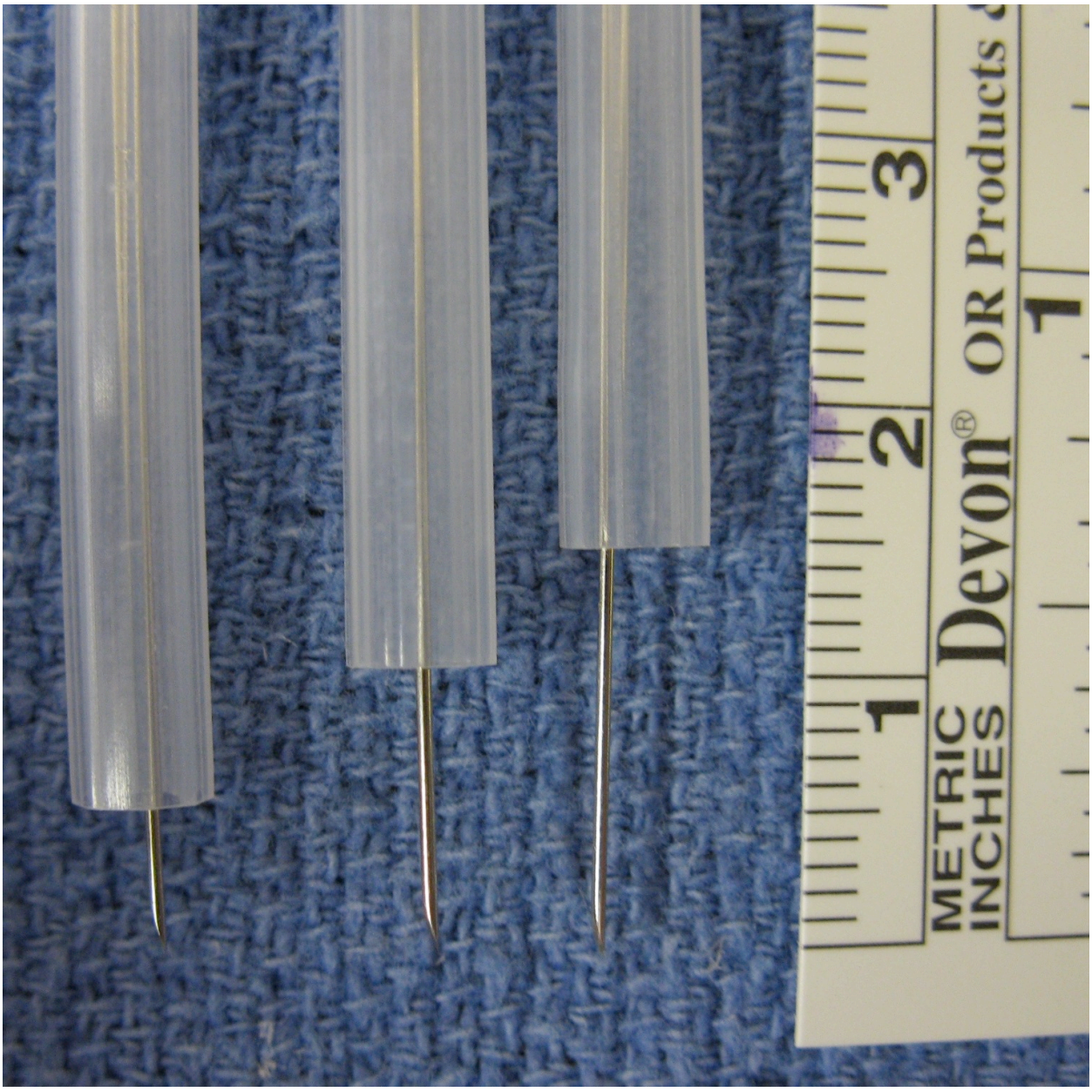

Figure 3.0.2 Photograph of compress modification

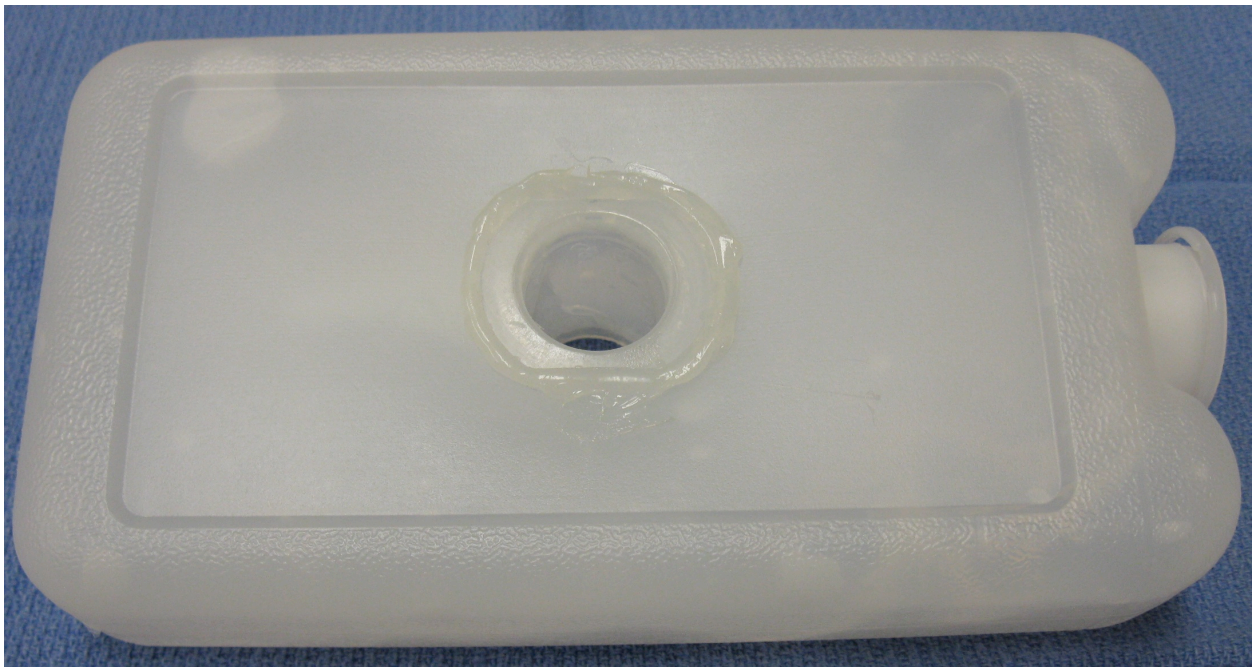

Figure 3.0.3 Photograph of compress modification

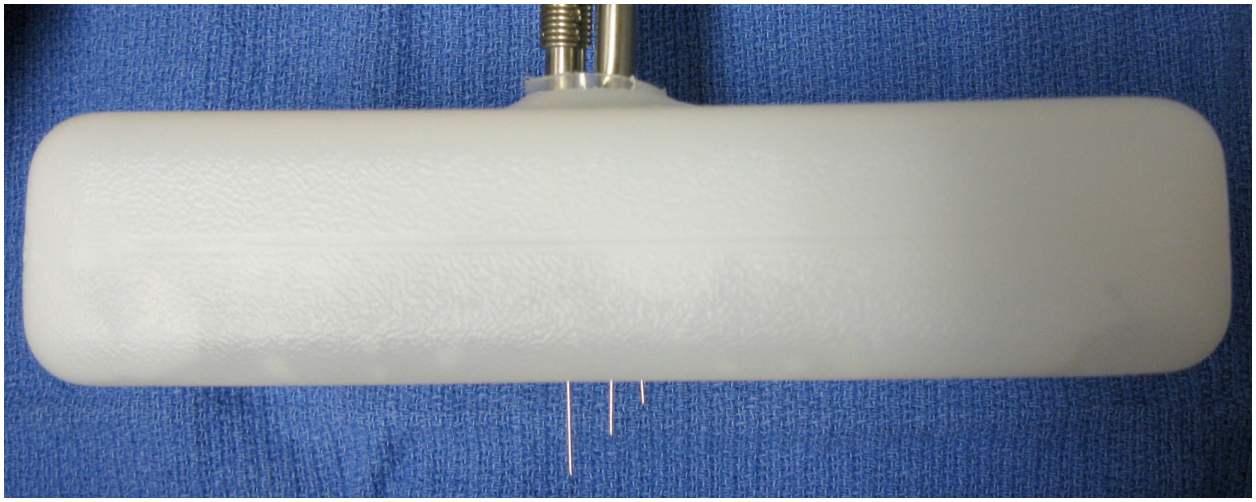

Figure 3.0.4 Cold compress temperature change

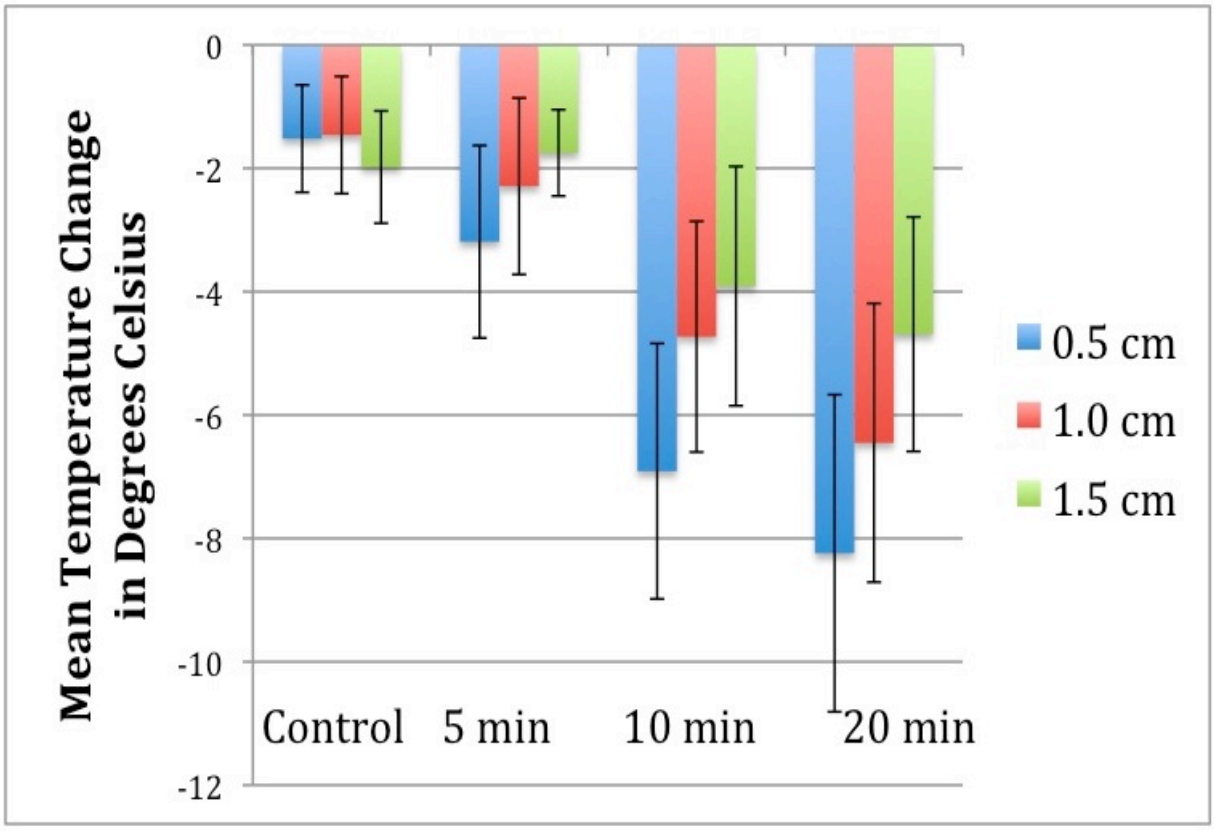

Figure 3.0.5 Warm compress temperature change

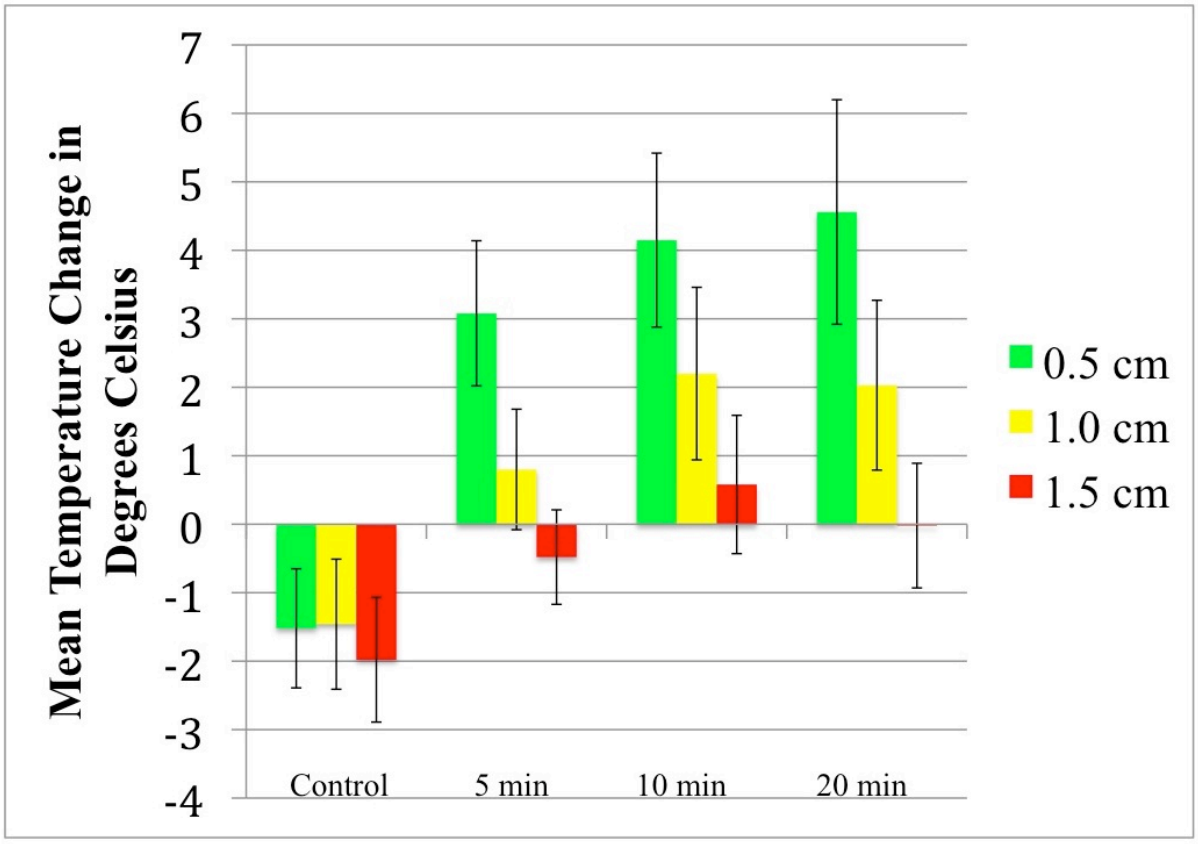

Figure 3.0.6 Cold compress 5 minutes

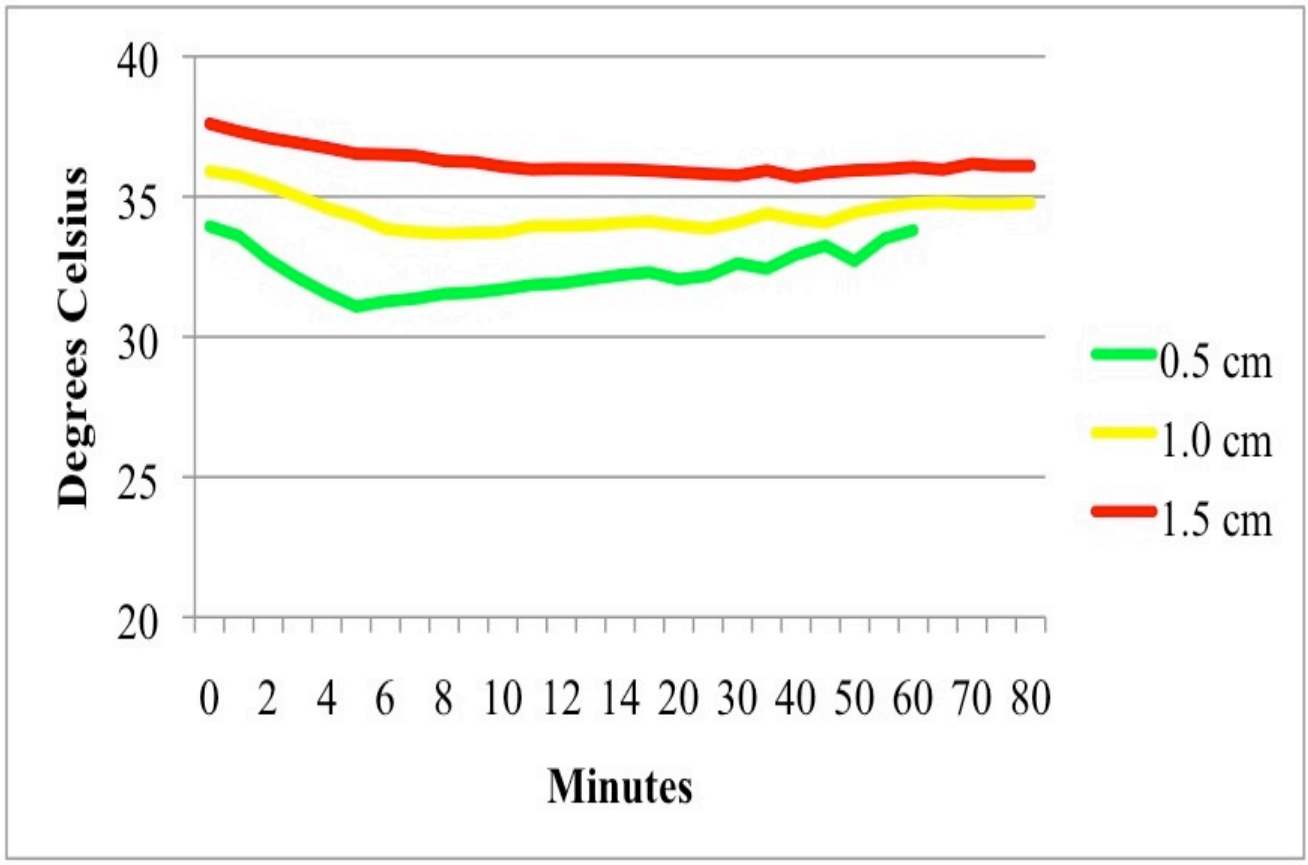

Figure 3.0.7 Cold compress 10 minutes

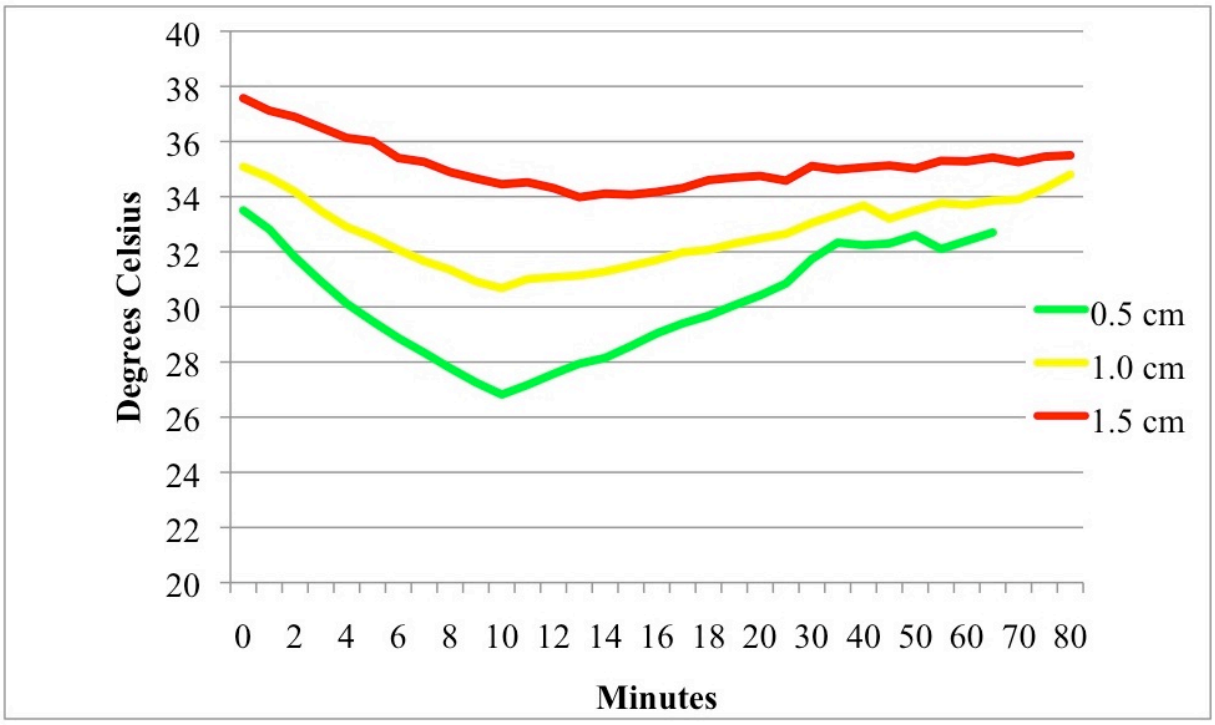

Figure 3.0.8 Cold compress 20 minutes

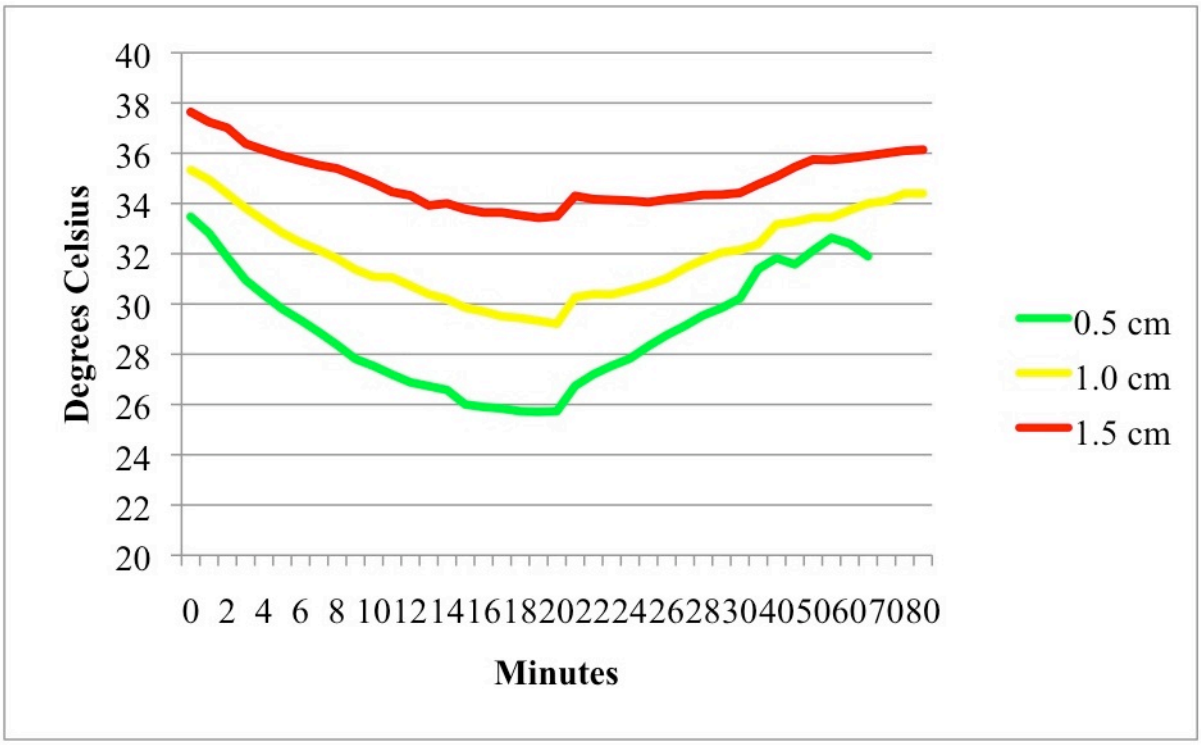

Figure 3.0.9 Warm compress 5 minutes

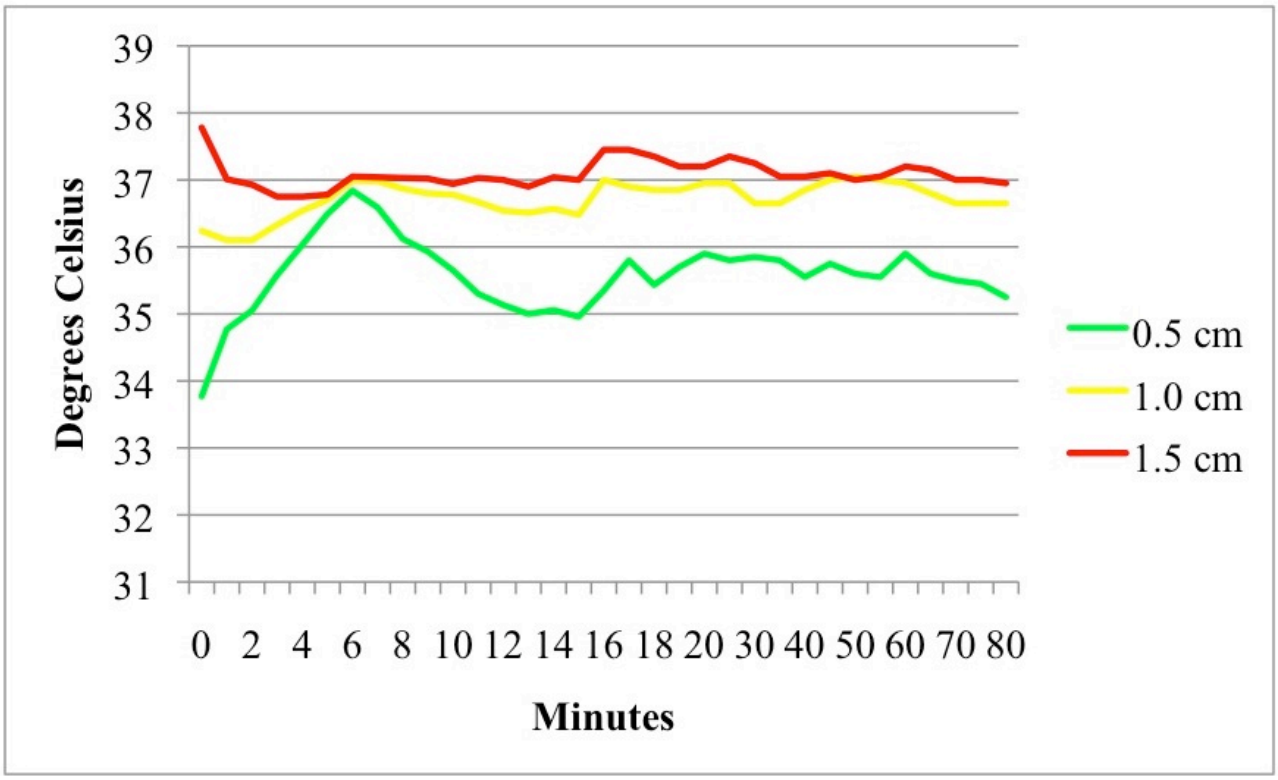

Figure 3.10 Warm compress 10 minutes

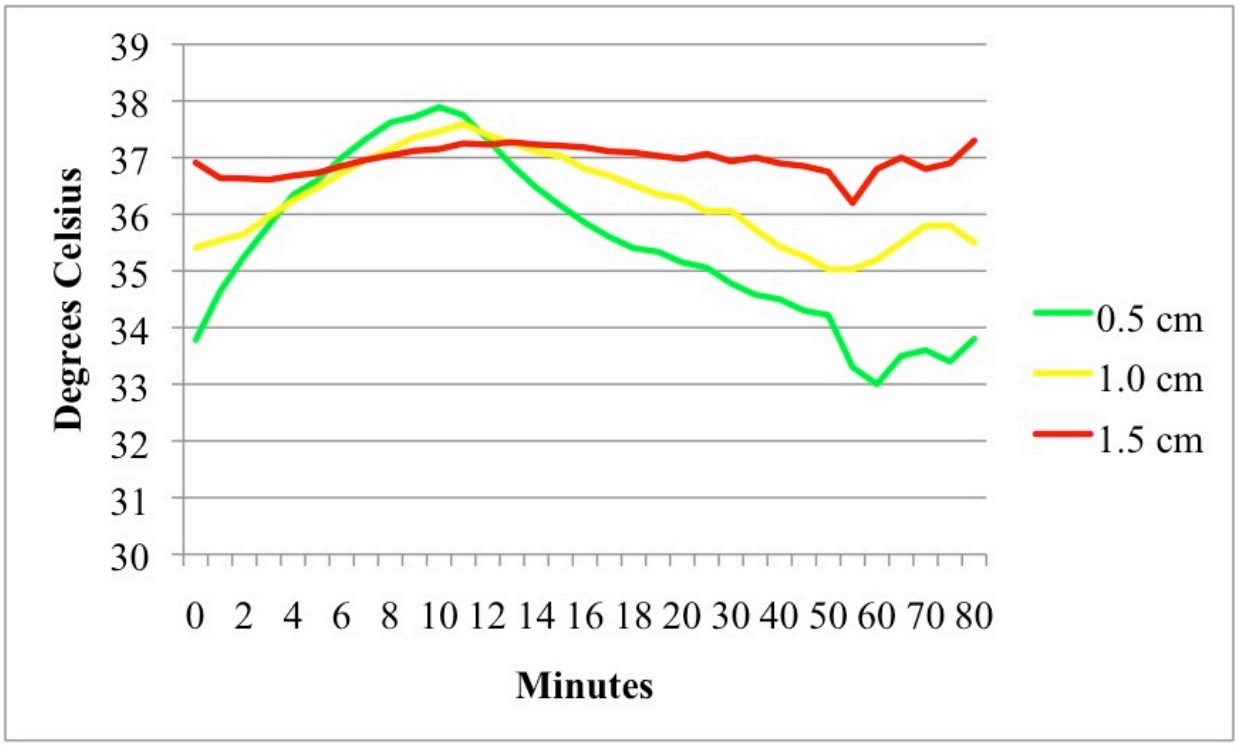

Figure 3.11 Warm compress 20 minutes

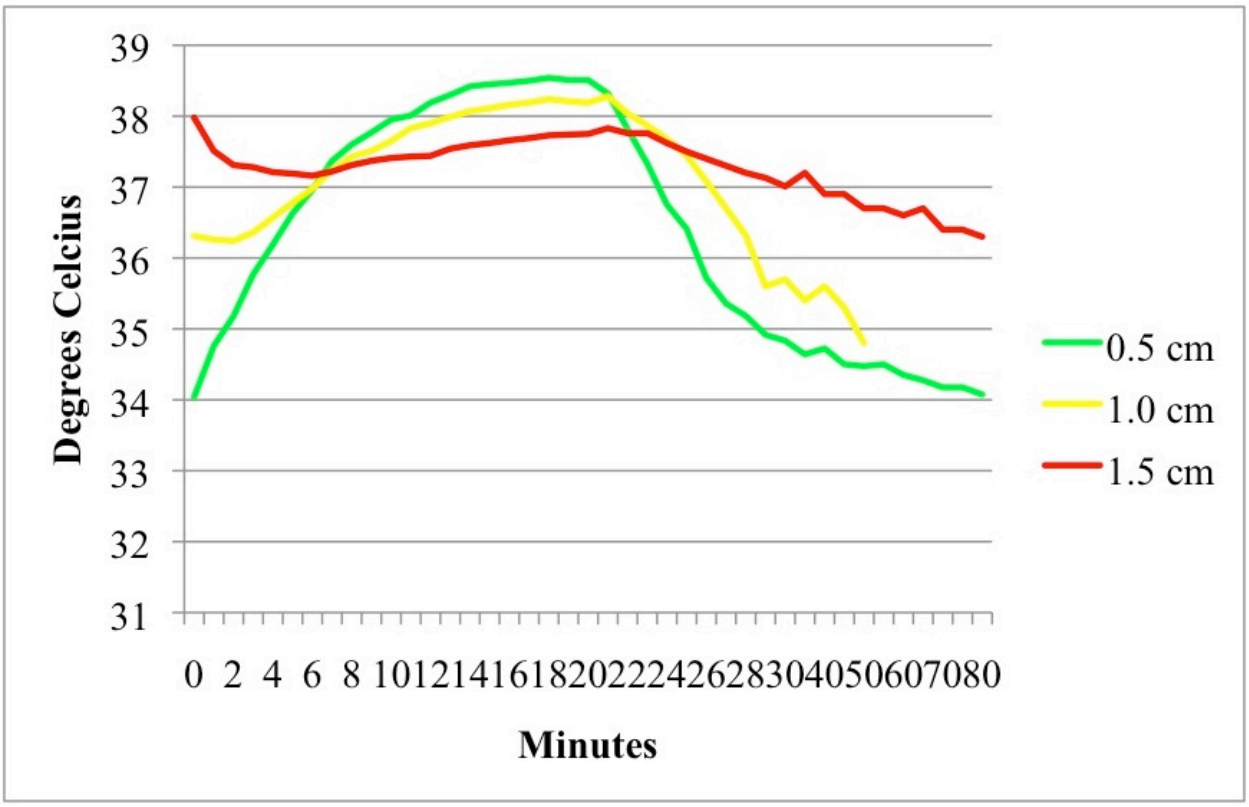

Table 3.1 Mean temperature change cold compress

Tissue Depth (cm)	Control	5 min	10 min	20 min
0.5	-1.52±0.87[c]	-3.19±1.56[a]	-6.91±2.07[b]	-8.24±2.57[b]
1.0	-1.46±0.95[b]	-2.29±1.43[b]	-4.73±1.87[a]	-6.45±2.26[c]
1.5	-1.98±0.91[b]	-1.75±0.7[b]	-3.91±1.94[a]	-4.69±1.9[a]

Table 3.2 Mean temperature change warm compress

Tissue Depth (cm)	Control	5 min	10 min	20 min
0.5	-1.52±0.87	3.08±1.06[a]	4.15±1.27[b]	4.56±1.64[b]
1.0	-1.46±0.95	0.8 ±0.88[a]	2.2±1.26[b]	2.03±1.24[b]
1.5	-1.98±0.91	-0.48±0.69[a]	0.58±1.01[b]	-0.02±0.91[ba]

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