การเปลี่ยนแปลงของการไหลเวียนเลือดและอุณหภูมิผิวหนังบริเวณขาส่วนล่างในการตอบสนองต่อ การใช้ความเย็นในชายวัยกลางคนถึงวัยสูงอายุ

นางสาว เสาวภา ธุมาพันธ์

# สถาบนวิทยบริการ

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต สาขาวิชาเวชศาสตร์การกีฬา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปีการศึกษา 2549 ลิขสิทธิ์ของจุฬาลงกรณ์มหาวิทยาลัย

# CHANGES OF LOWER – LEG BLOOD FLOW AND SKIN TEMPERATURE IN RESPONSE TO COLD APPLICATION IN MIDDLE AGED TO ELDERLY MEN

Miss Saowapa Thumapun

# สถาบนวทยบรการ

A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Science Program in Sports Medicine Faculty of Medicine Chulalongkorn University Academic Year 2006 Copyright of Chulalongkorn University

Thesis Title	CHANGES OF LOWER - LEG BLOOD FLOW AND SKIN
	TEMPERATURE IN RESPONSE TO COLD APPLICATION IN MIDDLE
	AGED TO ELDERLY MEN.
Ву	Miss Saowapa Thumapun
Field of Study	Sports Medicine
Thesis Advisor	Assistant Professor Sompol Sanguanrungsirikul, M.D., MSc.
Thesis Co-advisor	Assistant Professor Onanong Kulaputana, M.D., Ph.D.

Accepted by the Faculty of Medicine, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master 's Degree

Kamduta Lee..... Dean of the Faculty of Medicine

(Professor Pirom Kamolratanakul, M.D., MSc.)

THESIS COMMITTEE

Chairman

(Associate Professor Prasong Siriviriyakul, M.D.)

Sompol Somewary mile Thesis Advisor

(Assistant Professor Sompol Sanguanrungsirikul, M.D, MSc.)

Manay Colopatore Thesis Co-advisor

(Assistant Professor Onanong Kulaputana, M.D., Ph.D.)

maipon Somboon Member

(Associate Professor Juraiporn Sombunwong, M.D., MSc.)

Wannet k. ..... Member

(Wasuwat Kitisomprayoonkul, M.D.)

เลาวภา ธุมาพันธ์ : การเปลี่ยนแปลงของการไหลเวียนเลือดและอุณหภูมิผิวหนังบริเวณขา ส่วนล่างในการตอบสนองต่อการใช้ความเย็นในชายวัยกลางคนถึงวัยสูงอายุ. (CHANGES OF LOWER – LEG BLOOD FLOW AND SKIN TEMPERATURE IN RESPONSE TO COLD APPLICATION IN MIDDLE AGED TO ELDERLY MEN) อ. ที่ปรึกษา: ผศ.นพ. สมพล สงวนรังศีริกุล, อ.ที่ปรึกษาร่วม : ผศ.พญ.ดร. อรอนงค์ กุละพัฒน์, 61 หน้า.

การปฐมพยาบาลเบื้องต้นที่ใช้ในการรักษาอาการบาดเจ็บแบบเฉียบพลันของกล้ามเนื้อใน ปัจจุบันนั้น ยังคงยึดหลักการ RICE สำหรับปฏิบัติทั้งในคนวัยหนุ่มสาวและคนวัยสูงอายุ อย่างไรก็ตาม ยังไม่พบรายงานการศึกษาเกี่ยวกับการตอบสนองของการไหลเวียนเลือดและอุณหภูมิผิวหนังต่อการใช้ ความเย็นในการรักษา โดยเฉพาะอย่างยิ่งในกลุ่มของคนวัยสูงอายุ การศึกษาในครั้งนี้จึงมีวัตถุประสงค์ เพื่อศึกษาความแตกต่างของการไหลเวียนเลือดและอุณหภูมิผิวหนังบริเวณขาส่วนล่างในการ ตอบสนองต่อการใช้ความเย็นในขายวัยกลางคนถึงวัยสูงอายุ โดยมีผู้เข้าร่วมการศึกษาทั้งสิ้น 250 คน ในกลุ่มขายวัยหนุ่มมีอายุระหว่าง 18 – 35 ปี (24.7 ± 4.4 ปี) และในกลุ่มขายวัยสูงอายุ มีอายุระหว่าง 42 – 85 ปี (61.6 ± 8.5 ปี) การศึกษาครั้งนี้ใช้การประคบน้ำแข็งซึ่งบรรจุในถุงพลาสติก ร่วมกับการห่อ ด้วยผ้าขนหนูชุบน้ำที่อุณหภูมิห้อง บิดพอหมาด ก่อนที่จะนำมาประคบบริเวณเหนือตาตุ่มข้างช้ายด้าน ใน 15 ซม. เป็นระยะเวลา 20 นาที ทำการบันทึกการเปลี่ยนแปลงของการไหลเวียนเลือดและอุณหภูมิ ผิวหนังบริเวณขาส่วนล่างทุกๆ 1 นาที

ผลการศึกษา พบว่า อุณหภูมิผิวหนังบริเวณขาส่วนล่างในทั้ง 2 กลุ่ม มีแนวโน้มการลดลงแบบ เดียวกันขณะประคบน้ำแข็ง โดยพบความแตกต่างของการลดลงของอุณหภูมิผิวหนังระหว่างกลุ่มชาย วัยหนุ่ม (15.2 ± 2.7°C) และชายวัยกลางถึงวัยสูงอายุ (16.4 ± 2.6°C) อย่างมีนัยสำคัญในนาทีที่ 20 (p<0.001) โดยในกลุ่มชายวัยหนุ่ม (17.5 ± 2.3°C) มีการลดลงของอุณหภูมิผิวหนังมากกว่าชายวัย กลางคนถึงวัยสูงอายุ (15.7 ± 2.3°C) สำหรับการเปลี่ยนแปลงของการใหลเวียนเลือดนั้น ไม่พบว่ามี การเปลี่ยนแปลงอย่างมีนัยสำคัญในทั้งสองกลุ่ม จากการศึกษาครั้งนี้ สามารถสรุปได้ว่า ชายวัยหนุ่มมี การตอบสนองต่อการประคบน้ำแข็งดีกว่าชายวัยกลางคนถึงวัยสูงอายุ และการลดลงของอุณหภูมิ ผิวหนังไม่มีความสัมพันธ์กับการเปลี่ยนแปลงของการใหลเวียนเลือดในระหว่างการประคบน้ำแข็งทั้ง ในกลุ่มชายวัยหนุ่มและวัยกลางคนถึงวัยสูงอายุ

	เวขศาลตร์การกีฬา	ลายมอขอนสต			1/
ปีการศึกษา					
		ลายมือชื่ออาจารย์ที่ปรึกษา	เร่วม	1 garmel	

##4774793030 : MAJOR SPORTS MEDICINE

KEY WORD: COLD APPLICATION / LOWER – LEG BLOOD FLOW / SKIN TEMPERATURE
 SAOWAPA THUMAPUN : CHANGES OF LOWER – LEG BLOOD FLOW AND SKIN
 TEMPERATURE IN RESPONSE TO COLD APPLICATION IN MIDDLE AGED TO
 ELDERLY MEN. THESIS ADVISOR : ASST. PROF. SOMPOL SANGUANRUNGSIRIKUL,
 M.D., MSc. THESIS COADVISOR : ASST. PROF. ONANONG KULAPUTANA,
 M.D., Ph.D., 61 pp.

Ice, compression, and elevation are the basic principles of acute soft tissue injuries management. Few clinicians, however, can give specific evidence based guidance on the appropriate recommendation especially for the elderly because no literatures regarding local vascular response and skin temperature during cold application have been reported. The objective of this study was to examine leg arterial blood flow and skin temperature in response to cold application in middle aged to elderly men (OLD group) compared to young men (YOUNG group). Two hundred and fifty healthy men participated as subjects ranging in age for the YOUNG group from 18 - 35 years ( $24.7 \pm 4.4$  years) and 42 - 85 years ( $61.6 \pm 8.5$  years) for the OLD group. An ice pack was wrapped in a wet towel before applied to the left ankle overlying the medial malleolus for 20 minutes. Leg arterial blood flow using venous occlusion strain gauge plethysmography and skin temperature using tele – thermometer were recorded in every minute of cold application.

The result showed that the skin temperatures were continuously decreased during cold application in both groups. There was a significant difference in skin temperature between YOUNG group (15.2  $\pm$  2.7°C) and OLD group (16.4  $\pm$  2.6°C) at the end of cold application (p< 0.001). The YOUNG group demonstrated a greater drop in skin temperature than the OLD group (17.5  $\pm$  2.3°C vs 15.7  $\pm$  2.3°C). However, a significant difference in blood flow reduction from baseline was not observed between YOUNG and OLD group. In conclusion, the reduction in skin temperature did not coincide with the decrement in leg blood flow for both young and middle aged to elderly men when cryotherapy was applied for a period of up to 20 minutes.

#### ACKNOWLEDGEMENTS

The success of this thesis can be attributed to the extensive support and assistance from my advisor, Assistance Professor Sompol Sanguanrungsirikul, M.D., MSc. and my co – advisor, Assistance Professor Onanong Kulaputana, M.D., Ph.D. I deeply thank them for their valuable advice and guidance in this research. I wish to thank to Associate Professor Prasong Siriviriyakul, M.D., Associate Professor Juraiporn Somboonwong, M.D., MSc., and Wasuwat Kitisomprayoonkul, M.D. for their suggestions in this study.

I also wish to express my special thanks to all of my friends at Sports Medicine unit, Department of Physiology, Faculty of Medicine, Chulalongkorn University for their kindness and co – operation during this study.

I am grateful to the entire volunteers for their participation as subjects in this study. Finally, I am grateful to my family for their support, entire care, and encouragement throughout this study.

สถาบันวิทยบริการ จุฬาลงกรณ์มหาวิทยาลัย

## TABLE OF CONTENTS

ABSTRACT (TH	HAI)	iv
ABSTRACT (EI	NGLISH)	V
	GEMENTS	
	NTENTS	
LIST OF TABLI	ES	ix
LIST OF FIGUR	RES	х
CHAPTER		
I.	INTRODUCTION	1
	BACKGROUND AND RATIONALE	1
	RESEARCH QUESTION	3
	OBJECTIVES	
	ASSUMPTIONS	
	LIMITATIONS	5
	OPERATIONAL DEFINITION	5
	EXPECTED BENEFITS AND APPLICATIONS	6
II.	REVIEW LITERATURES	7
	ACUTE SOFT TISSUE INJURIES	7
	CRYOTHERAPY IN THE MANAGEMENT	
	OF ACUTE SOFT TISSUE INJURIES	8
	AGING	18
	ACUTE INJURY IN ELDERLY	24
111.	RESEARCH METHODOLOGY	26
	POPULATION AND STUDY SAMPLES	26
	INCLUSION CRITERIA	26
	EXCLUSION CRITERIA	26
	INSTRUMENTS	28

### TABLE OF CONTENTS

CHAPTER		
III.	RESEARCH METHODOLOGY	
	COLD APPLICATION	30
	SKIN TEMPERATURE MEASUREMENT	30
	LEG BLOOD FLOW MEASUREMENT	31
	THERMAL SENSATION TEST	34
	AUTONOMIC FUNCTION TEST	35
	PROCEDURE	36
	DATA ANALYSIS	37
IV.	RESULTS	38
	BASELINE CHARACTERISTICS OF THE SUBJECTS	39
	RESPONSES OF LOWER – LEG BLOOD FLOW	41
	RESPONSES OF LEG SKIN TEMPERATURE	44
	THE RELATIONSHIP BETWEEN SKIN TEMPERATURE	
	REDUCTION AND LEG BLOOD FLOW	48
V.	DISCUSSION AND CONCLUSION	50
	DISCUSSION	50
	CONCLUSION	55
REFERENCES		56
BIOGRAPHY .		61

# จุฬาลงกรณ์มหาวิทยาลัย

### LIST OF TABLES

TABLE	PAGE
4.1 Baseline characteristics of the subjects	39
4.2 Lower – leg blood flow over 20 minutes of application	43
4.3 Lower – leg blood flow response to cold application	
(using skin temperature cut off point)	44
4.4 Lower – leg skin temperature over 20 minutes of application	46
4.5 Number of subjects in each group that response to cold	
application (using skin temperature at 20 <sup>th</sup> minute as cut off point)	47
4.6 Mean skin temperature responses at 20 <sup>th</sup> minute of cold	
application in YOUNG and OLD groups	47

สถาบันวิทยบริการ จุฬาลงกรณ์มหาวิทยาลัย

### LIST OF FIGURES

FIGURES	PAGE
3.1 Subject starting position	29
3.2 YSI tele – thermometer (Yellow Springs Instrument Co., Inc, Ohio, USA)	
with a factory calibrated thermister surface probe	31
3.3 Tele – thermometer calibration equipment	31
3.4 EC6 strain gauge plethysmography	32
3.5 Lower – leg blood flow measurement	33
3.6 Heart rate variation during deep breathing test	36
4.1 Systolic blood pressure changes during 20 minutes of	
cold application in YOUNG and OLD men	40
4.2 Diastolic blood pressure changes during 20 minutes of	
cold application in YOUNG and OLD men	40
4.3 Heart rate changes during 20 minutes of cold application	
in YOUNG and OLD men	41
4.4 Lower – leg blood flow response to 20 minutes of cold application	
in YOUNG and OLD men	42
4.5 Lower – leg skin temperatures response to 20 minutes of cold	
application in YOUNG and OLD men	45
4.6 Correlation between lower – leg skin temperature and blood flow	
reduction in YOUNG men	48
4.7 Correlation between lower – leg skin temperature and blood flow	
reduction in OLD men	49

# CHAPTER I

#### Background and Rationale

Participation in sports – related activities increases the risk for acute soft tissue and musculoskeletal injuries. A thorough assessment is required for accurate diagnosis and provides a guide for appropriate treatment. Initial management is based on the principles of basic first aid: rest, ice, compression, and elevation (Prentice and Arnheim, 2000). Both physiologic and clinical evidence suggests that cryotherapy can reduce nerve conduction velocity (Lee and Warren, 1978), decrease local blood flow (Taber et al., 1992; Weston et al., 1994), and suppress cellular metabolic rate (Rivenburgh, 1992). These effects, in turn, reduce the inflammatory reaction to trauma (Cameron, 1999), lessen pain (Ohkoshi and Nagasaki, 1999), retard edema formation (Deal et al., 2002), and reduce secondary hypoxic injury (Merrick and Rankin, 1999). The evidence from the systematic reviews suggests that melting iced water applied through a damp towel for 20 minutes is most effective (Ohkoshi, 1992; Holcomb, 1996; MacAuley, 2001).

Although cryotherapy has been promoted in the immediate and rehabilitative care of soft tissue injury, the basis for its application at each stage is quite different. Immediately post injury, ice is principally used to reduce metabolism, thereby minimizing secondary hypoxic injury and the degree of tissue damage. In contrast, when applied for rehabilitative purposes, it is used primarily to relieve pain, which facilitates earlier and more aggressive exercise. Currently, many clinicians do not fully understand the pathophysiological rationale at each stage and may not be using it to its full advantage (Jutte and Merrick, 2001; MacAuley, 2001; Otte, 2002).

There are several factors affecting the effectiveness of cryotherapy: method and duration of application, the depth of subcutaneous fat, size of the area being treated, the physical properties of the cryotherapy modalities (e.g. size, weight), and even the temperature gradient between the target tissue and the cooling modalities. In addition, cryotherapy is commonly combined with compression and elevation, making it difficult to determine the value of cryotherapy alone (Brooks and Fashey, 1988). Moreover, studies that have addressed the effectiveness and the physiological in to cryotherapy have only used young animal or human thermoregulatory model (Thompson, Holowatz and Kenney, 2005); very little is known regarding how cold application affects in aged human.

Aging is a normal biologic process (Robergs and Roberts, 1997). Most physiological functions decline with age, so the mobility of the elderly is more difficult and reflects the increasing rate of soft tissue injuries (Brooks and Fashey, 1988). There are marked changes in body composition and structure with age. Body weight increases steadily beginning in the twenties and continues to increase until about 55 or 60 years old, when it begins to decline (Brooks and Fashey, 1988). Height decreases gradually (Brooks and Fashey, 1988). Weight gain is accompanied by increased body fat and decreased lean body mass (Brooks and Fashey, 1988). Males advance from an average of 15% fat at 17 years to about 28% at 60 (Brooks and Fashey, 1988). Women change from about 25% at 17 years old to about 39% at 60 years old (Brooks and Fashey, 1988).

It is difficult to pinpoint the effects of aging on the cardiovascular system. Deconditioning and disease also play significant roles in changes in the cardiovascular system overtime (Robergs and Roberts, 1997). Aging causes a normal reduction in total body water (Brooks and Fashey, 1988). As part of this, there is less fluid in the bloodstream, so blood volume and muscle blood flow also decreases (Brooks and Fashey, 1988). Older persons also show decreased baroreceptor reflex sensitivity – that is, cardiovascular responses to changes in intravascular volume are altered. Such changes may put older persons at a greater risk for inappropriate volume expansion and may also contribute to the higher prevalence of orthostatic hypotension in the elderly (Olive and Devan, 2002).

Many neurophysiological changes occur with aging; the principal changes include decreased visual acuity, hearing loss, senses of taste and smell, touch sensitivity, and also decreased in reaction time. Aging causes many significant structural and functional alterations in the human body, which in turn can limit participation in daily activities of the elderly (Robergs and Roberts, 1997).

In addition, the rise in elder sports injuries outstrips the 8% increase in the number of Americans in this age group over the same period, notes the agency. "The increase in injuries is most likely attributable to increasingly active lifestyles and to increase participation in sports activities by other Americans", accords to the report (Sports injuries rising in the elderly, 2001). The study showed that between 1990 and 1996, sports – related injuries increased much more among older active people than among younger age groups. In contrast to the 54% increase noted in those over age 65, sports-related injuries increased by 18% in the 25 to 64 age group. In actual numbers, there were 34,000 sports injuries in the 65 and older age group in 1990, rising to 53,000 in 1996. "The increased incidence of injury occurred not only among the youngest of the report". Sports – related injuries to persons 75 and older increased by 29%. The report also noted that in both 1990 and 1996, about 60% of sports injuries in the geriatric age group occurred in men and the lower extremities are the most susceptible to injury (Sports injuries rising in the elderly, 2001).

It should be noted that the misuse of cryotheropy can cause tissue and nerve damage such as skin burn (O'Toole and Rayatt, 1999), frostbite, and superficial nerve palsy (Knight, 1995; Merrick, 2000). Surprisingly, the same acute soft tissue injury management is currently applied in both young and elderly despite they have different physiological changes and potential differences in response to cryotherapy. Nonetheless, there are limited numbers of literatures regarding physiologic response to cryotherapy in elderly reported. This study examined the changes of lower – leg blood flow and skin temperature in response to cold application in middle aged to elderly men.

#### Research question

Do the changes of lower – leg blood flow and skin temperature in response to cold application in middle aged to elderly men differ form the young men?

#### Objectives

1. To examine the changes of lower – leg blood flow in response to cold application in middle aged to elderly men.

2. To examine the changes of skin temperature at lower – leg in response to cold application in middle aged to elderly men.

#### Hypotheses

1. The changes of lower – leg blood flow in response to cold application in middle aged to elderly men differ from the young men.

2. The changes of skin temperature at lower – leg in response to cold application in middle aged to elderly men differ from the young men.

#### Scope of research

This study is an experimental research design which the middle aged and elderly men participated as subjects.

The study approval was obtained from the University Ethics Committee. Written inform consent was obtained from each subject before the experiment started. On attendance, subjects were given a briefing on the experimental procedure and risk involved, and reminded of their right to withdraw at any stage.

#### Assumptions

1. The equipments were calibrated for standard accuracy and reliability.

2. All volunteers participated as subjects in this study with voluntariness.

3. All subjects were asked to refrain from consuming alcohol, caffeine or food for an hour and having no vigorous activities for 2 hours before the session.

#### Limitations

1. The healthy young and middle aged to elderly men participated as subjects who were recruited following the inclusion criteria.

2. This study did not perform in the subjects who had a history of sudden trauma in the lower – leg, so the application in real acute soft tissue injury may show slightly different result.

#### Operational definition

1. Cold application is defined as the placement of cold pack to the subject's left ankle. In this study, the ice was enclosed in a plastic bag so that the surface area was 23 X 14 cm. and the total weight was 1 kg. To apply the ice pack to the subject's left ankle for 20 minutes, the ice pack was wrapped in a 100% cotton towel that had been soaked in room temperature water ( $25 \pm 1^{\circ}$ C) and wrung out as much water as possible before wrapping.

2. Lower – leg blood flow is defined as the total blood flow rate measured at the left leg using venous occlusion strain gauge plethysmography.

3. Skin temperature is defined as the surface temperature recorded at the skin of left lower – leg 15 cm above the left medial malleolus using thermistor probe of Tele – thermometer.

4. Middle aged men are defined as the male volunteers ranging in age from 45 – 65 years old in this study.

5. Elderly is defined as the older men aged 65 years old or higher.

#### Expected benefits and applications

1. Understanding the responses to cold application in middle aged to elderly men.

2. Providing recommendation for an optimal ice treatment protocol in middle aged to elderly men.

3. Providing recommendation for the duration of ice application for middle aged to elderly men.

4. Providing the preliminary data for further research.



# สถาบันวิทยบริการ จุฬาลงกรณ์มหาวิทยาลัย

### CHAPTER II REVIEW LITERATURES

#### Acute soft tissue injuries

Participation in sports – related activities increases the risk for acute injury to soft tissues. In adults, the sites most often affected include the ankle, knee, and wrist joint structures, along with the muscles of the back and extremities. The subsequent inflammatory response to tissue damage results in pain and swelling, which limits mobility. A thorough patient assessment is required for accurate diagnosis and provides a guide for appropriate treatment (McGriff, 2003).

#### Soft tissue responses to injury

In order to develop an appropriate early management programmed, it is necessary to have an understanding of the concepts of the response to injury, the mechanisms of healing and those processes that may be affected by what is, or is not, included in the management programmed. Once the concepts of tissue healing and repair are appreciated, it is easier to establish principled management programmed. These programs must be based on biochemical time-scales and must also consider the healing tissue's ability to withstand specific stresses and how it optimally responds to these stresses (Anderson and Hall, 1995).

When the body sustains an injury, it undergoes an organized and consistent process at the site of injury in its attempts to heal the area. Injury is the medical term for cellular damage. In a sprain, strain, bruise or crush, the local network of blood vessels is damaged, and oxygenated blood can no longer reach the tissues, causing some cells to die. The damaged blood vessels bleed, so the injured tissue contains dead cells, extracellular substance and extravasated blood (Evans, 1980). Although there may be some differences among the various structures, due to differences in vascularity, the overall process is essentially the same whether the injury is to ligament, tendon or muscle tissue. The primary differences in acute trauma are determined by the size and severity of injury and whether the injury must heal by primary or secondary intention.

#### Cryotherapy in the management of acute soft tissue injuries

The initial management of soft tissue injury is based on the principles of basic first aids: rest, ice, compression, and elevation (Prentice and Arnheim, 2000). Ice (or other applications of cryotherapy) has been recognised as one of the least expensive and widely used therapeutic modalities employed in the management of acute musculoskeletal injuries (Knight, 1989). Moreover, Knight further noted that the confusion surrounding cryotherapy is almost as extensive as its popularity, with different opinions existing concerning its theoretical base, techniques of application and the physiological responses of the body to its application.

The physiologic and biologic effects of cryotherapy are due to the reduction in temperature in the various tissues, together with neuromuscular actions (Airaksinen and Kyrklund, 2003). The clinical evidence suggests that cold application can reduce nerve conduction velocity (McMeekan and Murray, 1984), decrease local blood flow (Cobbold and Lewis, 1956), and suppress cellular metabolic rate (Sapega and Heppenstall, 1988). These effects, in turn, reduce the inflammatory reduction to trauma (Cameron, 1999), lessen pain (Bugaj, 1975; Ohkoshi and Nagasaki, 1999), retard edema formation (Deal and Tipton, 2002), and reduce secondary hypoxic injury (Merrick and Rankin, 1999).

Despite consensus about the physiologic effects of cryotherapy, there is no strong evidence to justify the use of cryotherapy modality over the others. A number of published studies (Myrer and Meason, 1998; Zemke and Anderson, 1998; Chesterton and Foster, 2002; Merrick and Jutte, 2003) have been performed to establish the critical level of tissue cooling required for specific effects. For instance, cold – induced analgesia begins after the localized skin temperature lowers to approximately  $13.6^{\circ}$ C (Bugaj, 1975), to reduce nerve conduction velocity (NCV) by approximately 10%, a temperature of  $12.5^{\circ}$ C is required (Knight, 1976; McMeeken and Murray, 1984), to lower metabolic enzyme activity by approximately 50%, tissue temperatures between  $10^{\circ}$ C –  $11^{\circ}$ C are suggested (Knight, 1976; Zachariassen, 1991). Thus, there is evidence that the optimum temperature range for reduction of cell metabolism without causing cell damage is in the range  $10^{\circ}$ C –  $15^{\circ}$ C (Sapega and Heppenstall, 1988).

The current recommendations in standard textbooks on the clinical use of cryotherapy also have many shortcomings (MacAuley, 2001) and most physicians rely on empirical evidence. The selection of parameters in a clinical environment continues to be made pragmatically, and recommendations in review articles range from 10 to 20 minutes 2 to 4 times per day (Kellnet, 1986), up to 20 to 30 minutes (Swenson et al., 1996), or 30 to 45 minute every 2 hours (Knight and Brucker, 2000). The most recent surveys of clinical practice have identified variations on the optimal mode, duration, and frequency of ice application (Johannsen and Langberg, 1997; Kerr and Daily, 1999) yet such factors dictate the degree of cooling (MacAuley, 2001) and the potential effectiveness of treatment. In addition, ice is commonly combined with compression and elevation, making it difficult to determine the value of cryotherapy alone (Meeusen and Lievens, 1986; Rivenberg, 1992; Thorsson, 2001).

Although cryotherapy has been promoted in the immediate (Knight, 1989; Swenson et al, 1996) and rehabilitative care of soft – tissue injury (Rivenburg, 1992), the basis for its application at each stage is quite different. Immediately post injury, ice is principally used to reduce metabolism, thereby minimizing secondary hypoxic injury and the degree of tissue damage (Knight, 2000). In contrast, when applied for rehabilitative purposes, it is used primarily to relieve pain, which facilitates earlier and more aggressive exercise (Knight, 2000). Currently, many clinicians do not fully understand the pathophysiological rationale at each stage and may not be using it to its full advantage (Knight, 2000). However, the evidence from the systematic review suggests that crushed iced water applied through a wet towel for 20 minutes is most effective (MacAuley, 2001).

A number of published studies have been performed the effectiveness of cryotherapy compared with other treatments.

#### Ice compared with heat/contrast bath

There was some evidence that cryotherapy was more effective than thermotherapy after ankle injury. Cote et al (1988) found that ice submersion with simultaneous exercises was significantly more effective than heat and contrast therapy combined with simultaneous exercises, at reducing swelling between 3 and 5 days post ankle sprain.

#### Ice compared with ice and Electrical Stimulation

Michlovitz et al (1988) compared the effect of ice alone to ice and simultaneous high – voltage electrical stimulation after acute ankle sprains. There was no significant difference when comparing ice alone and ice combined with low – frequency electrical stimulation (28 pulses per second) in terms of swelling, pain, and range of motion. Similarly, there was no significant difference comparing ice alone and ice combined with higher frequency electrical stimulation (80 pulses per second) in terms of swelling, pain, and range of motion.

#### Ice compared with no ice

Ice alone seems to be more effective than applying no form of cryotherapy after minor knee surgery. Levy et al (1997) compared the effect of an intermittent icing protocol combined with knee exercises to exercises alone, after minor arthroscopic knee surgery. The application of ice immediately before a rehabilitation program significantly decreased pain as measured by the affective component of the McGill Pain Questionnaire. The study also reported that subjects applying cryotherapy used significantly less prescription and nonprescription analgesia and had a significantly better weight bearing status; however, insufficient data are provided for the calculation of an effect size. In contrast, there were no significant differences between groups in terms of knee girth and knee range of motion 1 week post – surgery.

#### Ice (continuous) compared with ice (intermittent)

Using subjects' post – carpal tunnel release (CTR), Hochberg (2001) compared the effect of continuous cryotherapy to intermittent 20 – minute ice applications over the first 3 postoperative days. Subjects applying continuous cryotherapy had a significantly greater decrease in pain and wrist circumference in comparison to those using cryotherapy intermittently. This was the only study to compare the effectiveness of two different cryotherapy protocols, and although it appears that continuous cryotherapy should be the treatment of choice after surgery, the modes of cryotherapy application were not consistent across the two groups.

#### Ice and compression compared with no ice

There is marginal evidence that a single simultaneous treatment with ice and compression is no more effective than no cryotherapy after an ankle sprain. Laba (1989) found that a single application of ice and compression, in addition to standard rehabilitation treatment (ultrasound, mobility, and proprioceptive exercises), produced similar levels of swelling and pain immediately post treatment and at discharge when compared to those receiving standard treatment only. Sloan et al (1989) also found that a single application of simultaneous ice and compression was as effective as no treatment in terms of reducing pain, swelling, and range of motion post ankle sprain. Similarly, Edwards et al (1996) found that the continuous use of ice and compression had similar benefits to no treatment in terms of improving pain and range of motion when applied post surgically.

#### Ice and compression compared with ice alone

Only one clinical study has compared ice and compression to ice alone (Cohn et al., 1989). The combination of treatments appeared to be significantly more effective than ice in terms of reducing the amount of intramuscular and oral analgesia administered post – anterior cruciate ligament reconstruction. These results must be interpreted with caution, however, as the mode and duration of ice treatment was not controlled for across groups. Moreover, there are numerous studies have been reported the effects of cryotherapy.

#### The effects of cryotherapy on skin temperature

Measuring the effect of cryotherapy on skin temperature is relatively uncomplicated. Erbrall et al (1992), using skin telethermography, found that 5 minutes of cooling using a wet pack reduced skin temperature to 7.6°C, and that, after 10 minutes of cooling, the skin temperature was 5°C. Comparing wet ice, dry ice and cryogen packs, the mean skin temperatures recorded after 15 minutes were 12°C, 9.9°C and 7.3°C respectively with no change in temperature at 1 cm proximal or distal to any of the cooling agents. Holcomb et al (1996) found skin temperatures using the standard ice pack (1 kg ice in a plastic bag) of 19°C initially with a more gradual drop to 14°C at 30 minutes. Knight et al (1996) found an attenuation of the ice effect when applied following 15 minutes exercise but, of course, temperature changes within the muscle are of much more clinical importance (Hopper et al., 1997).

#### Depth of temperature reduction

There is evidence that the optimum temperature range for reduction of cell metabolism, without causing cell damage, is in the range of  $10^{\circ}C - 15^{\circ}C$  (Rivenburge, 1992) but there also may be a distinction between the use of ice in first aid treatment and in rehabilitation (Barnes, 1979)

### Duration of application

It is difficult to find definitive recommendations on the frequency and duration of cold application in the literature. Ho et al (1994) noted that few studies had examined the effects of cold on blood flow over time, and that those which had were performed on arms and fingers, and had produced no consensus. These researchers found decreases in soft tissue blood flow and skeletal blood flow with as little as five minutes ice application, which effects were enhanced three – to four – fold by increasing the duration of application to 25 minutes. This study supported earlier work by Knight et

al (1980), who also applied ice for 25 minutes. Belitsky et al (1987) found skin cooling of up to 12°C after 15 minutes application, with skin temperatures rising towards their pre – ice levels 15 minutes following removal of the ice. The effect of longer durations of application has not been established. Recommended frequency of application varies between 20 minutes in every hour (McMaster et al., 1978) to 30 minutes every two hours (Knight, 1989).

#### Application of different modalities

Cold can be applied in different ways. It may be applied directly, using proprietary ice packs, convenience frozen packs (e.g. frozen peas), and ice massage using ice in paper cups, frozen gel packs, chemical packs and topical coolants. The standard ice application of melting iced water ensures a constant temperature of 0°C. Ice taken straight from a freezer mat be below freezing point, and reusable gel packs may be as cold as -5°C to -15°C. If applied directly to the skin, these may cause tissue damage and frostbite. Deep penetration of cold is necessary to have any effect on muscle tissue thus topical sprays can have little effect.

Meeusen and Lievens (1986) have identified several modes of application of cold. The most common therapeutic application is usually with ice packs, ice towels or ice massage to the injured part (Kalenak et al., 1975 and Kern, 1980, cited Meeusen and Lievens, 1986). Another application technique, mostly used in research because of the ability to control temperature, is immersion in cold water. Local cryotherapy can also be applied by frozen gel packs, vapocoolant sprays, chemical ice and refrigerant inflated bladders/splints. Skin temperature has been reduced by between 6°C (ice pack) and 29.5°C (water immersion at 4°C) using different applications, applied for between ten seconds (vapocoolant spray) and 193 minutes (water immersion at 4°C). Intramuscular temperatures show a delayed fall in temperature that continues after the cold application has been removed (Meeusen and Lievens, 1986).

Few comparative studies have been carried out to evaluate the efficacy of different cold applications. However, McMaster et al (1978) compared chipped ice, frozen gel packs, chemical ice pack and an inflatable envelope containing a gaseous refrigerant, measuring deep intramuscular temperatures over a period of one hour, in canine thighs. The iced gel packs performed best of the artificial ice techniques but the chipped ice performed best overall, producing a temperature drop of 11.3°C. Belitsky et al (1987) also found crushed ice in a damp towel (wet ice) to be the most effective application, performing better than crushed ice in a plastic bag (dry ice) or cryogen packs, both in the actual temperature drop, and the duration of effect. These authors also found that the direct effects of the cold application were restricted to the area of application. Botte (1982, cited Meeusen and Lievens, 1986) found no depth effect with ethyl chloride sprays. Thus, the limited empirical evidence tends to support chipped ice as the most effective form of cold application.

#### Barrier effect

Ice is rarely applied directly to the skin, due to the risk of ice burns (Laing et al., 1973). Using a barrier between ice and the skin may however reduce the effect of ice application. LaVelle and Snyder (1985) compared the effect of commonly used protective barriers and found that, after 30 minutes ice application, the mean temperature was 30.5°C using a padded bandage, 20.5°C with a bandage alone, 17.8°C with a dry washcloth and 10.8°C with no barrier and 9.9°C with a damp washcloth. This has important clinical implications. There was little difference when ice was applied using a damp cloth barrier, compared with chipped ice in a plastic bag applied directly. Cold was not however conducted though a padded elastic bandage.

#### Effects of subcutaneous fat to skin temperature

In subjects with large subcutaneous deposits of fat, cooling may be impaired (Wolf and Basmajian, 1973). In a study in which deep muscle temperatures were recorded in the gastrocnemius muscle in ten subjects over a period of five minutes, the subject who was described as being "of a muscular body type" demonstrated the greatest temperature change, whilst the subject who was described as "obese" demonstrated the smallest temperature change. Although the sample size in the study was not large enough to draw definitive conclusions regarding the influence of obesity on cooling, it appears that longer periods of cooling may be required in obese individuals to achieve a therapeutic effect.

#### The effect of cryotherapy on blood flow

Tissue cooling produces an initial vasoconstriction in the cutaneous blood vessels, resulting in a decrease in local blood volume. Controversy has surrounded the subsequent responses, since Lewis (1930, cited Kowal, 1983) first described cyclic phases of skin cooling and rewarming (the "hunting response") when tissue temperature reached 15<sup>o</sup>C when a subject's finger was immersed in ice water.

Measurement of skin blood flow is usually accomplished by laser Doppler flowmetry or venous occlusion plethysmography (Johnson et al., 1984; Oberg, 1990; Johnson and Proppe, 1996). There is no absolute "gold standard" for measuring limb blood flow in humans (Joyner et al., 2001). Laser Doppler measurement of skin blood flow is based on the Doppler shift of incident laser light when it is reflected off moving red blood cells (Oberg, 1990). This method offers the advantages of high temporal resolution (measurements can be taken continuously) and specificity to the cutaneous microcirculation (Oberg, 1990; Saumet et al., 1988). The disadvantages of this method include the inability to measure absolute flow values (i.e. flow is measured in arbitrary Laser Doppler units or volts rather than in milliliters per minute) and the restriction to a relatively small area of measurement. The former disadvantage is often overcome by normalizing Laser Doppler flowmetry values to values measured during maximal vasodilation (with either local warming of the skin or local sodium nitroprusside) (Charkoudian and Johnson, 1999; Kellogg et al., 1998).

Venous occlusion plethysmography can be used to measure blood flow in the forearm, lower – leg, or finger. In the forearm or the lower leg, it can be used to measure changes in skin blood flow in situations in which blood flow to underlying muscle does not change (i.e. passive heat stress). In the finger, the contribution of muscle blood flow is much lower; however, this measurement includes areas of both glabrous skin (palmar side) and nonglabrous skin (dorsal aspect) (Johnson et al., 1995), which can limit data interpretation, depending on the issue being addressed. Venous occlusion plethysmography can be used to measure absolute changes in skin blood flow (e.g. with body heating) but has the disadvantages of not being specific to the skin (if muscle blood flow changes, data can be difficult to interpret) and providing discontinuous measurements (usually at most 4 measurements per minute).

Knight and Londeree (1980) measured blood flow using strain gauge plethysmography in 12 normal subjects during therapeutic applications of heat, cold and exercise. They found that total blood flow was greater (p<0.002) during a combination of cold and exercise than during application of heat. However, there was neither cold – induced vasodilation nor a reflex vasodilation following 25 minutes of cold application, suggesting that during cryotherapy it is exercise that causes the increased blood flow rather than the application of cold.

Similarly, Baker and Bell (1991) found no significant decrease in blood flow with either application of an ice pack or ice massage. Ho et al (1994) performed one of the most interesting studies, using triple phase technetium bone scans, and concluded that the temperature response in a joint is related to the temperature of the ice, the length of time of cooling, the patient's body temperature and skin temperature.

Blood flow studies are variable and, although there is usually vasoconstriction in the skin following ice application, there may be an increase in skin blood flow immediately following local ice application. Known as the "hunting reflex", this is a physiological reflex action to protect tissue from ice damage (Clarke et al., 1958). Kellett (1986) discussed this in his review quoting Pappenheimer (1948) and Barcroft (1943). The theoretical basis for this effect is that ice causes vasoconstriction, which helps reduce haemorrhage, but when temperature reduction is so low that it may compromise tissue viability, there is a reflex vasodilation. Hence, vasoconstriction and vasodilation may alternate in a 15 – 30 minute cycle.

Taber et al (1992) measured blood flow in 13 normal subjects, fewer than three experimental conditions of rest, application of a room temperature gel pack and application of a cold gel pack. A significant reduction in local blood volume was found for the cold gel pack, with the maximum decrease occurring 13.5 minutes after application. No reactive vasodilation was observed. Meeusen and Lievens (1986) suggested that research into the effect of application of cold on blood flow has produced conflicting reports and also reported the inconsistent findings from a number of studies on the effects of cold application on blood flow, suggesting that the differences in outcome are a result of the variation in methodologies used.

Cold therapy appears to be effective and harmless, and few complications or side effects have been reported after its use. Case reports indicate that there is a risk of nerve damage if the application is prolonged, or over superficial nerve trunks, or in athletes who have little subcutaneous fat. Covington and Basset (1993) and Basset et al (1992) reported six case studies in which peripheral nerve injury followed application of ice, and Green et al (1989) also reported a case study involving peripheral nerve injury following ice application. The nerve most commonly affected was the common peroneal nerve following ice application over the lateral aspect of the knee (four cases), although the lateral femoral cutaneous nerve was implicated in two cases when ice had been applied over the anterior superior iliac spine. The supraclavicular nerve was affected in one case following ice application over the shoulder. Durations of application varied between 20 minutes and one hour. The precise mode of application of ice was noted in only two cases (plastic ice bag and ice bag over a towel). This evidence, obtained from clinical observations, suggest that caution is required when applying ice in close proximity to superficial nerves.

#### Recommendations for guidelines

However, although the evidence is not conclusive, there is general agreement that the application of ice (or cold) for 20 – 30 minutes results in decreased pain, blood flow and metabolism (McMaster et al., 1978; Knight, 1989; Taber et al., 1992; Ho et al., 1994). Duration of application should be reduced over superficial nerve

trunks, or in patients with little subcutaneous fat (Basset et al., 1992; Covington and Basset, 1993), but increased in individuals with large subcutaneous deposits of fat (Wolf and Basmajian, 1973). The most effective mode of application of cold appears to be crushed ice enclosed in a plastic bag and wrapped in a damp towel that had been soaked in room temperature water and wrung out as much water as possible before wrapping (Ohkoshi, 1992; Holcomb, 1996; MacAuley, 2001).

#### Aging

Aging is a normal biologic process. All multicellular organisms undergo changes with time. The progression of development, reproductive maturity, and aging has been extensively investigated in the biologic sciences. Most physiologic functions do decline with age but different extents, and there are several theories as to why the aging process occurs.

#### The physiologic changes of aging

Aging is associated with functional and structural changes in the ability of the cardiovascular system to adapt to physiological stress (Giannattasio and Ferrari, 1994; Monahan and Dinenno, 2001). Skin blood flow responses to thermoregulatory stresses decrease with aging (Pierzga et al., 2003). Furthermore, baroreflex control of peripheral circulation in response to changes in arterial and/or central blood volume also decreases with aging (Shi et al., 1996), and aging is associated with an increased susceptibility to orthostatic hypotension (Smith and Porth, 1991).

Vascular alterations in structure and function due to aging could also contribute to determined thermoregulation through impaired blood flow (Borisov and Huang, 2000). Decreased capillary density (Coggan et al., 1992) and a thickening of vascular walls (Moreau et al., 1998) are present with aging.

Vascular function is altered with aging and may influence muscle blood flow. Altered vascular function in older individuals is evidenced as impaired endothelial function (DeSouza and Shapiro, 2000; Singh and Prasad, 2002), an altered ratio of endothelium receptors (Ergul et al., 1998), and/or altered reactivity of the smooth muscle to sympathetic activity (Moreau and d'Uscio, 1998). Reduced endothelial function is related to impaired formation and decreased activation of Nitric oxide and is particularly prominent in older subjects with evidence of cardiovascular disease, diabetes, or obesity (William et al., 1996).

These structural and functional alterations in the vascular system may explain age associated reductions in muscle blood flow. Decreased leg blood flow and vascular conductance are present in elderly compared to young subjects during whole body exercise (Proctor et al., 1998) and in response to reactive hyperemia. Decreased basal limb blood flow was related to increase vasoconstriction in the elderly compare to younger individuals. Discrepancies in aging effects on muscle blood flow may be due to the use of active or inactive subjects. In addition, it is not clear whether the age related changes in blood flow were a result of reduced cardiac output or reduced local vascular capacity. These inconsistent findings of reduced blood flow in older subjects suggest that other age – associated factors are involved (Olive et al., 2002).

#### Age and body temperatures in the cold

It is generally believed that older persons are less able to maintain core temperature during a cold challenge than younger persons. Survey type studies have indicated that hypothermia is more prevalent among older than younger persons. Fox et al (1973) found that 10 % of the elderly (>65 years) living in their own homes in England had a low core temperature (<35.5°C), as indicated by morning urine temperature. However, these results may not reflect direct effects of ageing alone.

Krag and Kountz (1950) exposed 13 older (57 – 91 years, 7 females, 6 males) patients and 6 younger (22 – 36 years, 3 males, 3 females) subjects to variable degrees of cold stress (5  $^{\circ}$ C – 15 $^{\circ}$ C). Each person was supposed to stay in the cold for 2 hours without clothes, but the actually times varied from 45 to 120 minutes. Although no statistical methods were used, most of the older subjects experienced a marked fall

in rectal temperature, whereas the younger subjects maintained their rectal temperature almost at pre-exposure levels.

O'Hanlon and Horvath (1970) exposed 34 men (17 – 54 years) to cold (8°C, air velocity 0.8 m/s) for 2 hours. They found that age and rectal temperature were not correlated before the experiment, but at the end of exposure the correlation coefficient was significantly positive. They concluded from correlation analysis that the older subjects maintained higher rectal temperature than younger subjects. However, most of the subjects were presumably rather young, because the mean age of the whole group was only 26.5 years.

A mild cold exposure  $(17^{\circ}C)$  for 30 minutes was used by Wagner et al (1987) to compare young men (19 – 29 years), and older men (46 – 67 years). During the exposure older men showed a slightly greater fall (-  $0.2^{\circ}C$ ) in rectal temperature than the younger men (-  $0.1^{\circ}C$ ).

A further study by the same group (Wagner et al., 1987) compared healthy older (51 – 72 years) and younger (20 – 30 years) men when exposed to  $10^{\circ}$ C for 2 hours with minimal clothing. Similar fall in rectal temperature (-  $0.2^{\circ}$ C) was observed in both groups, although the older subjects had greater body fat content. Study by Collins et al (1985) investigated two groups of healthy men with similar percentage of body fat. Younger (18 – 24 years) and older (63 – 70 years) subjects were exposed to  $6^{\circ}$ C (still air) for 2 hours. In the cold, rectal temperature fell, on the average, by  $0.4^{\circ}$ C in the older group and significantly less ( $0.1^{\circ}$ C) in the younger group. Similar finding was obtained by Mathew et al (1986) who exposed 9 different age groups of healthy men (n=15 in each group) to  $10^{\circ}$ C for two hours in shorts and vests. Their subjects had a fairly comparable body composition across the groups. The results indicated that after the age 45 years, the decline in oral temperature was greater than in the younger groups. Inoue et al (1992) also matched their younger (20 – 25 years) and

older subjects (60 – 71 years) by adiposity in their experiments, where the exposure consisted of 60 minutes rest at 17°C and 12°C. In their study, the older men were, however, over 10 kg lighter than the younger ones indicating a reduced muscle mass. During all cold exposures, a markedly greater fall in rectal temperature was observed in the older subjects compared to younger ones.

Falk et al (1994) included three groups of men, all matched for body weight, body surface area and subcutaneous fat thickness. Younger men (21 - 29) years) were compared with physically trained older men (55 - 70 years), whose aerobic capacity was similar to younger men. The third group comprised sedentary older men (55 - 70 years) whose aerobic capacity was lower compared to the other two groups. The design thus compared two groups of similar age but differing aerobic fitness, and two groups different in age but similar in aerobic fitness. In both of the older groups, rectal temperature decreased significantly more than in the younger men, when exposed to 30 minutes rest and 30 minutes exercise at air temperature of 5<sup>o</sup>C in shorts. Interestingly, during light bicycle exercise (50 W) the heat production was sufficient to maintain rectal temperature at a steady level in the younger but not in the older subjects.

Two studies (Bernstein, 1956; and Wagner, 1985) have focused on comparing younger and older women under cold stress. In contrast to men, older women in both studies were able to maintain rectal temperature as well as young women. These findings are confounded by the fact, that the older women in both studies had more fat and a smaller body surface area/mass ratio than the younger women.

Results on changes in skin temperature have been also as variable as results on core temperature changes. Changes in skin temperature under cold stress may indirectly indicate the degree of skin vasoconstriction. The study by Wagner (1974) employing exposures to cold less than 60 minutes have found higher skin temperatures in older subjects compared to younger subjects, whereas similar or greater declines were observed with longer exposures. Young and Lee (1997) suggested that the level of subcutaneous thickness might explain the age – related differences in mean skin temperature between studies.

Budd et al (1991) exposed a group of 12 men (26 - 52 years) to cold air ( $10^{\circ}$ C) for 2 hours in nude. Using a multiple regression model for analysis, they found that when differences in body fat were removed age was positively associated with a higher mean skin temperature and a lower insulation.

#### Age and peripheral circulation in the cold

In addition to whole – body exposures to cold, these effects have been studied also by using local cooling of hands, forearm and face. Spurr et al (1955) made finger temperature measurements during immersion of the hand in 10°C water on healthy subjects varying in age from 6 to 83 years. They found that the hunting reaction was seen less frequently in older subjects: it was observed in most of the young subjects but in none of the oldest subjects. The results indicated age-related changes in vascular reactivity.

Jennings et al (1993) used facial cooling during sleep in healthy younger (25 years) and older (over 80 years) female subjects in order to examine changes in finger skin temperature (centrally mediated). In response to cooling, finger skin temperature decreased significantly more in the young than in the older subjects indicating reduced peripheral vasoconstriction in the older subjects. During the experiments rectal temperatures were similar between the groups.

Venous occlusion plethysmography is a more direct estimate of changes in peripheral circulation than skin temperature and it has been used in some studies to measure finger and forearm blood flow. Under a mild exposure to cold air (17<sup>o</sup>C), older subjects reduced finger blood flow less than younger subjects (Wagner et al., 1974). Years later, Wagner et al (1985) obtained similar results on forearm blood flow when the cold exposure was more severe (2 hours at 10°C). Collins et al (1977) did a longitudinal study on older subjects (69 years or older), in which they measured hand blood flow responses to cold. Before the follow – up 37 out of 43 subjects exhibited a vasoconstrictor response to cold, but after 4 years only 29 subjects had maintained their vasoconstrictor response.

Kenney and Armstrong (1996) carefully matched younger (22 - 31 years) and older (58 - 67 years) subjects for subcutaneous fat thickness, total adiposity, body size and aerobic fitness. The subjects were first exposed to gradual air cooling (from  $28^{\circ}$ C to  $10^{\circ}$ C), which was then maintained for the remainder of the 2 hours experiment. The younger subjects revealed a decreased in forearm blood flow at a greater rate and to a greater extent than did the older group. No significant differences were found in changes of mean skin temperature and esophageal temperature during the cooling. Although the latter had a tendency to decrease in a faster rate in the older subjects. The authors concluded that older men have a diminished reflex limb vasoconstrictor response to skin cooling.

The problem with plethysmography is that it measures total regional circulation in a limb and does not separate skin circulation from blood flow to other tissues. Khan et al (1992) utilized laser – Doppler flowmetry to measure finger skin blood flow in 20 young and (mean age 26 years) and 28 older (mean age 68 years) subjects during transient cooling in a climatic chamber from 40°C to 12°C. All subjects were healthy. Vasoconstriction was rapid in young subjects, whereas in older subjects it was significantly slower. Also, the older subjects experienced less sympathetic vasoconstrictor bursts in the tracings. The results in the elderly were, however, quite variable some subjects showing a clear vasoconstrictor response to cooling and some had responses similar to the diabetic group examined indicating sympathetic dysfunction.

Richardson et al (1992) performed a more refined study by using laser – Doppler flowmetry combined with video densitometry to measure nailfold capillary blood cell velocity. The subjects were 10 younger (mean age 25 years) and 10 older (mean age 71 years) subjects, who immersed their hand and forearm in cool water (15°C) for 5 minutes. During the first minute of cooling both groups experienced a significant fall in skin blood flow in the contra lateral arm. During subsequent 4 minutes skin blood flow remained depressed in the younger subjects, but returned to pre – exposure levels in the older ones. Capillary blood cell velocity was also slightly depressed during cooling in the younger group but not in the older subjects. These results point out that the attenuated vasoconstrictor response in older individuals is more pronounced in the deeper vessels of skin.

#### Acute injury in elderly

Recent, there has been reviewed interest in the benefits of physical fitness. Over 60% of American adults do not engage in the recommended amount of physical activity. Therefore, public health initiatives such as National Physical Fitness and Sports Month have been implemented to promote exercise for improved fitness and overall wellbeing. As participation in athletic activities increases, there is an associated risk for acute soft tissue injury. This risk is particularly pronounced for inactive adults who abruptly inflate vigorous activity. These injuries include damage to muscles, tendons, and joint structures.

According to the National Institute of Arthritis and Musculoskeletal Disorder, ankle sprains are the most common injury in the United State. A sprain indicates a partial or complete stretching or tearing of ligaments within a joint. When a joint sustains a substantial force, as caused by a fall, sudden twist, or direct impact, ligament damage may occur.

It should be noted that the misuse of cryotheropy can cause tissue and nerve damage such as skin burn (O'Toole and Rayatt, 1999), frostbite, and superficial nerve palsy (Knight, 1995; Merrick, 2000). Surprisingly, the same acute soft tissue injury management is currently applied in both young and elderly despite they have different physiological changes and potential differences in response to cryotherapy. Nonetheless, there are limited numbers of literatures regarding physiologic response to cryotherapy in elderly reported.



# สถาบันวิทยบริการ จุฬาลงกรณ์มหาวิทยาลัย

# CHAPTER III RESEARCH METHODOLOGY

#### Research design

This study is an experimental research which examined the changes of lower-leg blood flow and skin temperature in response to cold application in middle aged to elderly men using venous occlusion strain gauge plethysmography and tele – thermometer.

#### Population

In this study, the 2 target population groups were Thai healthy middle aged to elderly men who were 40 years old or older, and young men aged 18 – 35 year. The study samples were recruited according to the following criteria.

#### Inclusion criteria

1. Being Thai men aged from 40 years old for middle aged to elderly subject and 18 – 35 years old for young subject.

2. Volunteers signed the consent form to become subjects.

3. Autonomic function test, using heart rate variation during deep breathing, was performed to ensure that all subjects had normal autonomic function.

#### Exclusion criteria

1. History of heavy smoking.

2. History of cardiovascular or peripheral vascular diseases; Raynaud's phenomenon, diabetes mellitus treated by insulin injection etc.

3. Neurological or muscular pathologies.

4. History of recent trauma or injury to the left ankle.

5. Presence of any soreness or open wounds on the left ankle.

6. Local hot or cold insensitivity/hypersensitivity.

7. Cryoglobulinemia

- 8. Paroxysmal cold hemoglobinuria
- 9. Allergy to cold
- 10. Thermoregulatory disorders
- 11. Autonomic nervous system dysfunction
- 12. Capillary refill time at big toe over 2 seconds (very fair skin)

13. Taking any medications that may affect heart rate and blood flow such as  $\beta$ -adrenergic blocking drugs, digitalis preparations, calcium channel blockers, diuretics,  $\beta_2$ -agonists, or anti-inflammatory drugs.

# Sample

# Sampling technique

This study used purposive sampling technique and voluntariness for recruiting subjects.

## Sample size determination

In this study, sample size determination was calculated from the previous pilot study in 14 middle age and elderly men aged from 45 years and 5 younger men ranging in age between 20 – 35 years participated as subjects. The pilot study was examined lower-leg blood flow and skin temperature in response to 20 minutes of cold application by using venous occlusion strain gauge plethysmography and tele – thermometer. The sample size was calculated from 2 – independent group formula

n = 
$$\begin{bmatrix} Z_{\alpha} \sqrt{2P_{1} (1 - P_{1}) + Z_{\beta} \sqrt{P_{1} (1 - P_{1}) + P_{2} (1 - P_{2})} \end{bmatrix}^{2}}$$

- $P_1$  = the different proportion of lower-leg blood flow at 20<sup>th</sup> minute compare with baseline in young group = 0.59
- $P_2$  = the different proportion of lower-leg blood flow at 20<sup>th</sup> minute compare with baseline in older group = 0.83
- $\alpha$  = 0.05 (two-sided), Z<sub> $\alpha$ </sub> = 1.96
- $\beta$  = 0.20 (two-sided), Z<sub> $\beta$ </sub> = 1.28
- $D = P_2 P_1 = 0.21$
- $n = [(1.96)\sqrt{(2)(0.59)(1-0.59)} + (1.28)\sqrt{(0.59)(1-0.59)} + (0.38)(1-0.38)]^2$

(0.21)<sup>2</sup>

n = 113.8

n for each group was 114 persons. To account for the expecting drop outs during the experimental and ensure the study confidence, subjects were added for 10% more. Thus, total subjects were 125 persons for each group.

Instruments

- 1. Case record form
- 2. Sphygmomanometer
- Venous occlusion strain gauge plethysmography (EC6, DE Hokanson Inc, WA, USA)
- 4. YSI tele-thermometer (Yellow Springs Instrument Co., Inc, Ohio, USA)

- 5. Crushed ice was enclosed in a plastic bag sized 23 X 14 cm. and weighed 1 kg.
- 6. 100% cotton towel sized 30 X 30 X 0.1 cm.
- 7. Test tube filled with  $40^{\circ}C 45^{\circ}C$  water and  $10^{\circ}C 15^{\circ}C$  water
- 8. Lange skinfold caliper (Cambridge Scientific Industries, Ltd, Cambridge, MD)
- 9. Knee and ankle support

# Subject starting position

Subject was in the supine position on the treatment bed and relaxed. The legs were extend, slightly external rotated and supported approximately 10 cm. above the heart level in order to lower the initial venous pressure, empty the venous system and facilitate outflow between the venous occlusion (Groothuis and Vliet, 2003) using a Styrofoam block to support the knee and ankle for comfort and to raise the center part of the calf to make room for the strain gauge (Alomari et al., 2004). Subjects were asked to have no leg movements and calf muscle contraction preventing gauge perturbance.



Fig 3.1 Subject starting position

### Cold application

Room temperature was maintained at  $25 \pm 1^{\circ}$ C throughout the test. The crushed ice was enclosed in a plastic bag so that its surface area was  $23 \times 14$  cm and the total weight was 1 kg. Air was evacuated from the bag in an attempt to improve conforming of the bag to the skin surface. Following 10 minutes of resting data collection, the ice pack was applied around the left ankle and the measurement of leg blood flow and skin temperature was continued for additional 20 minutes. To apply the cold pack to subject's ankle, the ice bag was wrapped in a 100% cotton towel that had been soaked in room temperature water ( $25 \pm 1^{\circ}$ C) and wrung out as much water as possible before wrapping.

### Skin temperature measurement

Leg skin temperature was measured by YSI tele – thermometer (Yellow Springs Instrument Co., Inc, Ohio, USA) with a factory calibrated thermister surface probe (Fig 3.2). The thermometer was displayed to a resolution of  $0.01^{\circ}$ C and calibrated by physiograph system (Biopac System Inc., CA, USA) with data acquisitions software (Acknowledge®version 3.7.5) (Fig 3.3). The accuracy is  $\pm 0.2^{\circ}$ C. A layer of self – adhesive felt 5 mm thick was fixed to the exposed portion of the probe to protect the measuring tip from the direct influence of the cold modality and measured only leg skin temperature not the temperature gradient or the ice bag temperature.



Fig 3.2 YSI tele – thermometer (Yellow Springs Instrument Co., Inc, Ohio, USA) with a factory calibrated thermister surface probe



Fig 3.3 Tele - thermometer calibration equipment

# Leg blood flow measurement

An EC6 strain gauge plethysmography was used to measure blood flow in the lower leg. Electrically calibrated strain gauge plethysmography is a system for measuring limb blood flow. The measurement system may also be referred as arterial inflow or venous occlusion plethysmography (Fig 3.4).



Fig 3.4 EC6 strain gauge plethysmography

A 4 – wire limb gauge was placed around the middle of the muscle, and two cuffs were placed around the leg, one above and one below the gauge. With every heart beat, blood is pooled in the area and the circumference of the limb changes. The venous return is occluded with a pressure that does not interfere with arterial blood flow. Strain gauge plethysmography measures the rate of change (slope) of the circumference of a limb. This slope is interpolated to represent change in limb volume by using the unit ml per 100ml/min, technically; this represents a change in the volume of the limb segment over a brief period of time rather than the change in blood flow. However, because the change in volume is assumed to be the result of arterial inflow of blood, the convention is to report the change as blood flow.

The parameters of the plethysmography were set according to the manufacturer guidelines. The reading interval (the period between readings) was set at 15 seconds, and the sample/inflow time (the amount of time between inflation and deflation of the thigh cuff) was set at 5 seconds. This setting allowed the plethysmography to automatically inflate and deflate the thigh cuff at the specified interval. The air pressure for the thigh cuff was set at 50 mmHg. This inflation pressure was sufficient to stop venous return from the leg while still allowing arterial inflow. The ankle cuff (arterial occlusion cuff) was quickly inflated to 50 mmHg above the subject's systolic blood pressure for 90 seconds then deflated for 30 seconds interval over the

experimental session. The vein mode was set on the plethysmography in accordance with the other settings. In this mode, the signal from the strain gauge is directly coupled to the recorder without any filters to distort the signal, which allows the instrument to record continuous changes in blood flow.

The EC6 strain gauge plethysmography is compatible with the Noninvasive Vascular Program (NIVP3) software that interfaces the laptop computer with the plethysmography. The NIVP3 software stores patient information and waveforms for arterial inflow measurements. Blood flow was measured by mercury – in – rubber strain gauge secured around the largest circumferential point of the left calf and connected to the plethysmography. The strain gauges ranged in size from 22 to 42 cm; this study used sizes that ranged from 30 to 36 cm. Accurate electric calibration requires that the gauge be 1 to 3 cm smaller than the circumference of the limb. The limb gauges are a double loop of mercury filled rubber that were placed around the calf. The end of the loop hooks over the gauge end and fits into the groove behind the black end piece. Use adhesive tape to secure the gauge in two places. One strip of tape should go over the gauge end and the other should secure the cable to the skin a few centimeters from the end. The purpose of the tape is to prevent movement of the wire from disturbing the gauge (Fig 3.5).



Fig 3.5 Lower – leg blood flow measurement

#### Thermal sensation test (Discriminative temperature)

Thermal sensation tests, performed by using test tube filled with  $40^{\circ}$ C –  $45^{\circ}$ C water and  $10^{\circ}$ C –  $15^{\circ}$ C water touched against the subject's leg (Hill and Petrucci, 2002), were made to ensure intact sensation around the test area and measured the ice bag before the session. If subjects could correctly discriminate between hot and cold, sensation was deemed to be intact.

This test is designed to see if the patient has the ability to distinguish between hot and cold. This test is necessary to decrease the risk of injury and to ensure intact sensation around the test area. If subjects could correctly discriminate between hot and cold, sensation was deemed to be intact.

a. Contraindicated for patients with receptive aphasia

b. Procedure:

1. Touch subject with test tubes filled with warm  $(40^{\circ}\text{C} - 45^{\circ}\text{C})$ and cool  $(10^{\circ}\text{C} - 15^{\circ}\text{C})$  water. Maintain contact with the subject for 3 seconds before asking for a response. Ask the subject to report if the sensation is warm or cold. A wash cloth or other instrument can be substituted for test tubes (Scully and Barnes, 1989; Lundy, 1998).

It is important that the amount of surface area the testing tool touches on the skin is the same so that non – thermal cues (touch/pressure) do not interfere with testing result. The use of "hot" and "cold" tap water provides a temperature difference that is adequate for the test. Variances in the patient's skin temperature at the time of the test could affect the outcome. Thermal stimuli evoke a response in small primary atterent fibers. Information about thermal gradients is conveyed to the brain primarily, if not exclusively, by the anterolateral pathway. This information may be localized by nerve impulses carried in the contralateral spinothalamic tract.

#### Autonomic function test

To test the cardiac autonomic function, EKG was recorded by the physiograph system (Biopac System Inc., CA, USA) with data acquisition software (Acknowledge®version 3.7.5) for calculated heart rate and beat to beat time interval (RR interval). Blood pressure was observed by an oscillometric blood pressure monitor (Space Lab Inc., USA).

After all surface electrodes had been placed, the subject underwent a battery cardiac autonomic function test. This battery composed heart rate variation during deep breathing, the Valsalva test, heart rate response to tilting, systolic blood pressure response to tilting and diastolic blood pressure response to sustained handgrip. This study performed only heart rate variation during deep breathing for Autonomic function screening.

#### Heart rate variation during deep breathing

The deep breathing test was performed in a subject and consisted of taking six deep breaths within 1 min in the sitting position. The longest and shortest RR intervals during each breathing cycle were selected. The heart rate difference was calculated from the mean maximum and minimum heart rates. A difference of  $\leq 10$  beats was regard as abnormal, a difference of 11 - 14 beats as borderline and a different of > 14 beats as normal. This study recruited all subjects who had normal autonomic function (Fig 3.6).

# จุฬาลงกรณมหาวทยาลย



Fig 3.6 Heart rate variation during deep breathing test

# Procedure

1. The subjects were asked to refrain from consuming alcohol, caffeine, or food for an hour and have no vigorous activities for 2 hours before the session to help stabilize extremity blood flow and maintain normal fluid.

2. On attendance, subjects were asked to change into shorts and sit for approximately 10 minutes; resting heart rate and blood flow were recorded. The left mid – calf circumference and skinfold thickness at medical side of left calf were measured and the lower – leg thermal sensation test was performed before the session was started.

3. The subject then assumed a supine position on a treatment table. To measure the leg blood flow, the inflation cuffs were secured around the left thigh and ankle. The appropriate size mercury – in – rubber strain gauge was fastened around the mid-calf area and secured with tape. Tele – thermometer probe was attached with the tape 15cm above the left medial malleolus.

4. During the experimental session, the subject's blood pressure and heart rate were repetitively measured at 5 – minute interval. Upon completion, with

normal vital sign and no evidence of skin damage, the subjects were allowed to leave the lab.

#### Data analysis

All results were expressed as the mean  $\pm$  S.D. The unpaired t-test was used to detect the differences between the young and older groups on all baseline variables. Differences on skin temperature response to cold application between two groups were determined by 2 x 5 ANOVA. Multiple comparisons were performed with Bonferroni correction for Post Hoc analysis. Chi – square test was used as appropriate to investigate the responses to 20 minutes of cold application between young and older individual subjects. In addition, Pearson's correlation was also performed to determine the relationship between mean skin temperature reduction and leg blood flow changes with cold application.

An alpha level of 0.05 was used to determine statistical significant. All analyses were performed on the Statistical Package for the Social Sciences version 13.0 (SPSS, Chicago, IL, USA).



# CHAPTER IV RESULTS

# Characteristics of the subjects

Two – hundred and fifty healthy men participated as subjects. All of 250 subjects were complete study.

Baseline characteristics of the subjects in the young (YOUNG group) and middle aged to elderly (OLD group) men were summarized in Table 4.1. Age of the 125 young subjects ranged from 18 - 35 years (mean  $24.7 \pm 4.4$  years) and the 125 older subjects aged from 42 - 85 years (mean  $61.6 \pm 8.5$  years). The OLD group were significant heavier and shorter than the YOUNG group. Both systolic and diastolic blood pressure and ankle systolic blood pressure were higher in the OLD group, while the pulse pressure is higher in the YOUNG group. Although calf skinfold thickness was not different, the OLD group had a larger calf circumference than the YOUNG group. Moreover, the YOUNG group also had higher lower – leg skin temperature and blood flow than the OLD group. Resting heart rate, ankle brachial index, and calf skinfold thickness were not different between the two groups. Room temperature was controlled between  $25 \pm 1^{\circ}$ C throughout the experiment.

	Grou		
Characteristics	YOUNG group	OLD group	p-value
	(n=125)	(n=125)	
Age (years)	24.66 ± 4.39	61.56 ± 8.54	
Weight (kg.)	63.78 ± 7.93	67.11 ± 7.90	0.001
Height (cm.)	171.63 ± 5.43	166.31 ± 5.40	0.000
Body mass index (kg/m <sup>2</sup> )	21.64 ± 2.35	24.27 ± 2.55	0.000
Resting heart rate (bpm.)	70.14 ± 9.54	70.13 ± 9.78	0.990
Systolic blood pressure (mmHg)	114.61 ± 8.22	123.48 ± 11.70	0.000
Diastolic blood pressure (mmHg)	72.19 ± 8.73	81.79 ± 9.21	0.000
Ankle systolic blood pressure (mmHg)	112.90 ± 13.88	124.31 ± 14.30	0.001
Pulse pressure (mmHg)	42.42 ± 9.81	41.69 ± 10.34	0.000
Ankle brachial index	1.00 ± 0.85	1.01 ± 0.92	0.324
Calf skinfold thickness (cm.)	11.03 ± 3.72	10.67 ± 3.71	0.444
Calf circumference (cm.)	34.49 ± 2.38	35.98 ± 1.73	0.001
Resting skin temperature ( <sup>o</sup> C)	32.62 ± 1.43	32.03 ± 1.08	0.000
Resting leg blood flow (ml/100ml/min.)	2.11 ± 0.82	1.89 ± 0.89	0.044

# Table 4.1 Baseline characteristics of the subjects

Values are mean  $\pm$  S.D, \*p < 0.05

### Baseline skin temperature and blood flow measurements

At rest, there were age group difference observed for baseline skin temperature and leg blood flow (p<0.05). The YOUNG group had a higher baseline skin temperature (p<0.001) and leg blood flow (p<0.05) than the OLD group (Table 4.1).

Figure 4.1, Figure 4.2, and Figure 4.3 revealed the systolic blood pressure, diastolic blood pressure and heart rate in response to cold application of both groups throughout the session.

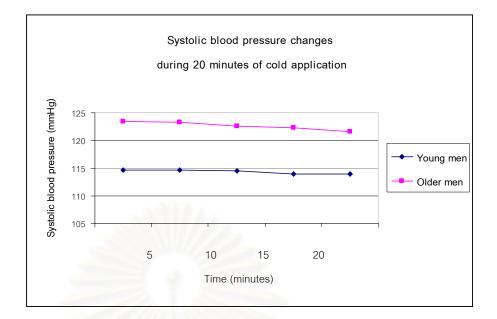
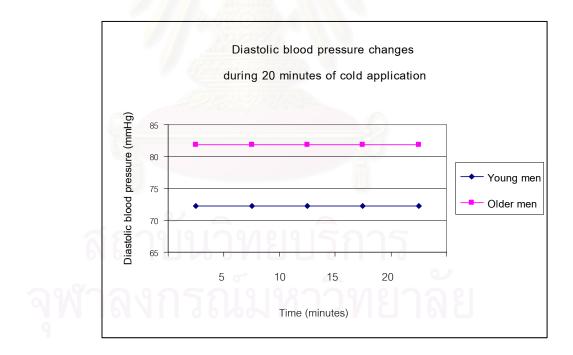
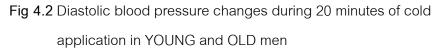
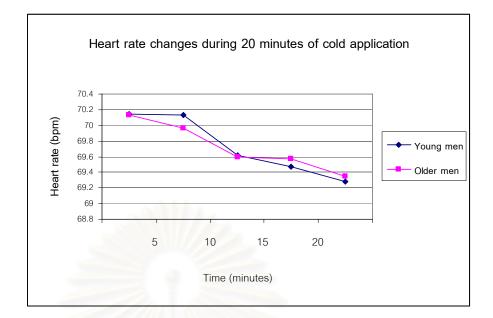
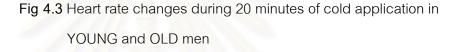


Fig 4.1 Systolic blood pressure changes during 20 minutes of cold application in YOUNG and OLD men









The results were divided into 3 sections: (1) leg blood flow response to cold application, (2) leg skin temperature during cold application, and (3) the relationship between leg skin temperature reduction and the decrement of leg blood flow.

# Lower - leg blood flow responses to cold application

The mean lower – leg blood flow recorded in every minute during cold application for two groups were summarized in figure 4.4. This showed that before the application, mean lower – leg blood flow in both YOUNG and OLD group was similar (2.11  $\pm$  0.82ml/100ml/min for YOUNG group and 1.89  $\pm$  0.89ml/100ml/min for OLD group).

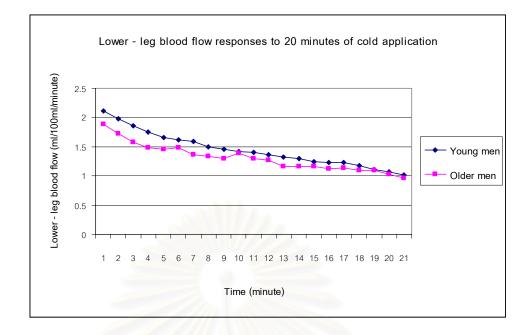


Fig 4.4 Lower – leg blood flow response to 20 minutes of cold application in YOUNG and OLD men

During cold pack application, lower – leg blood flow decreased immediately and rapid after ice application and continued to decrease gradually for the duration of the application in both groups. Moreover, there were significant within group reduction in lower – leg blood flow to 5<sup>th</sup>, 10<sup>th</sup>, 15<sup>th</sup>, and 20<sup>th</sup> minutes of application (p<0.001) for all comparisons, both group. Group differences of lower – leg blood flow in response to cold application were not statistically significant (Table 4.2).

	Lower – leg		
Time points	(ml/100ml	p-value	
	YOUNG group	OLD group	p-value
	(n=125)	(n=125)	
At baseline	2.11 ± 0.82	1.89 ± 0.89	0.022*
At 5 <sup>th</sup> minute of cold application	$1.62 \pm 0.77$	1.48 ± 0.80	0.078
At 10 <sup>th</sup> minute of cold application	1.40 ± 0.75	1.29 ± 0.74	0.248
At 15 <sup>th</sup> minute of cold application	1.23 ± 0.73	1.12 ± 0.70	0.122
At 20 <sup>th</sup> minute of cold application	1.02 ± 0.66	0.96 ± 0.67	0.251

Table 4.2 Lower – leg blood flow over 20 minutes of application

Values are mean ± S.D.

\* Significant difference with Bonferroni correction.

The absolute reduction of lower – leg blood flow for the entire trial in YOUNG group (1.09  $\pm$  0.54 ml/100ml/minute) was slightly greater than OLD group (0.93  $\pm$  0.52 ml/100ml/minute) (p<0.001). Although blood flow decreases measured during the session in OLD group were less than those measured in YOUNG group, the leg blood flow changes were not different between groups at the end of the application.

In addition, the subgroup analysis using the cut off point that skin temperature was lower or higher than  $15^{\circ}$ C had been suggested for effective treatment by cold application (Rivenburgh, 1992) found the results as follow. At the end of application, there was no difference in lower – leg blood flow between the YOUNG (1.04 ± 0.98 ml/100ml/min) and OLD group (0.98 ± 0.59 ml/100ml/min) whose skin temperature below  $15^{\circ}$ C (p=0.596). The YOUNG and OLD group whose skin temperature greater than  $15^{\circ}$ C showed similar mean lower – leg blood flow at 20 minutes of cold application (p=0.824) (Table 4.3).

# Table 4.3 Lower – leg blood flow response to cold application

# (using skin temperature cut off point)

	Lower – leg blood flow at 20 <sup>th</sup> minute of cold application			
	(ml/100ml/minute)			
Group	Lower than 15 °C		More than 15 <sup>°</sup> C	
	Lower – leg blood flow	p-value	Lower – leg blood flow	p-value
	(ml/100ml/min)		(ml/100ml/ninute)	
YOUNG group	1.04 ± 0.62	0.596	$0.98 \pm 0.74$	0.824
OLD group	0.98 ± 0.59		0.95 ± 0.17	0.024

# Leg skin temperature during cold application

The mean skin temperature was summarized in figure 4.5. In both groups, the skin temperatures were continuously decreased during cold application. Both group illustrated a similar pattern of skin temperature reduction, in which a sharp reduction occurred within the first few minutes after the application. After 20 minutes of application, the mean skin temperature had decreased substantially to  $15.17 \pm 2.69^{\circ}C$  for the young group, and  $16.43 \pm 2.57^{\circ}C$  for the older group. Throughout the 20 minutes of cold application period, the YOUNG group demonstrated a greater drop in skin temperature than the OLD group.

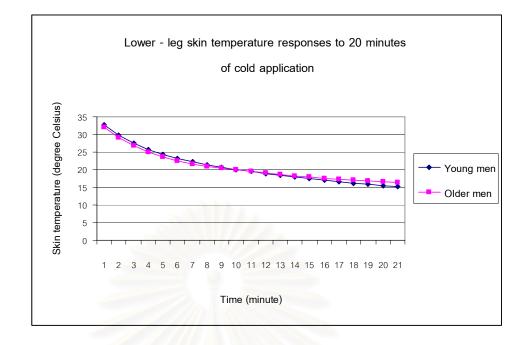


Fig 4.5 Lower – leg skin temperatures response to 20 minutes of cold application in YOUNG and OLD men.

ANOVA showed a significant difference in temperature response to cold application between the two groups (p<0.01). Post hoc analysis with Bonferroni correction showed a higher baseline skin temperature in the YOUNG group (p<0.01) (Table 4.4). However, the OLD group showed a greater skin temperature at 20 minutes of cold application (p<0.000).

	Skin temper		
Time points	YOUNG group	OLD group	p-value
	(n=125)	(n=125)	
At baseline	32.62 ± 1.43	32.03 ± 1.08	0.001*
At 5 <sup>th</sup> minute after cold application	23.22 ± 2.51	22.61 ± 2.27	0.023
At 10 <sup>th</sup> minute after cold application	19.46 ± 2.67	19.46 ± 2.52	0.495
At 15 <sup>th</sup> minute after cold application	17.00 ± 2.73	17.61 ± 2.55	0.035
At 20 <sup>th</sup> minute after cold application	15.17 ± 2.69	16.43 ± 2.57	0.000*

 Table 4.4 Lower – leg skin temperature over 20 minutes of application

Values are mean ± S.D.

\* Significant difference with Bonferroni correction.

At 20 minutes, a significant reduction in skin temperature from baseline was  $17.45 \pm 2.27^{\circ}$ C in YOUNG group (p<0.001) and  $15.68 \pm 2.34^{\circ}$ C in OLD group (p<0.001). In addition, the result from the YOUNG and OLD group showed that there were significant decreases in skin temperature at 5<sup>th</sup>, 10<sup>th</sup>, 15<sup>th</sup>, and 20<sup>th</sup> minutes of cold application (p<0.001 for all time points in both groups).

Due to the cut off point that skin temperature was lower or higher than  $15^{\circ}$ C; subsequent analysis using Chi – square test was performed. There were 76 subjects (60.8%) in YOUNG group and 38 subjects (30.4%) in OLD group that their skin temperatures were lower and equal to  $15^{\circ}$ C. For individuals with skin temperature below  $15^{\circ}$ C, the mean skin temperatures were  $13.47 \pm 1.36^{\circ}$ C in YOUNG group, and  $13.79 \pm 0.98^{\circ}$ C in OLD group. On the other hand, there were 49 subjects (39.2%) in YOUNG group and 87 subjects (69.6%) in OLD group that their skin temperatures were higher than  $15^{\circ}$ C. For this condition, mean skin temperatures were  $17.81 \pm 2.04^{\circ}$ C in YOUNG group and  $17.58 \pm 2.17^{\circ}$ C in OLD group (Table 4.5).

Table 4.5 Number of subjects in each group that response to coldapplication (using skin temperature at 20<sup>th</sup> minute as cut offpoint)

Group	Skin temperature at 20 <sup>th</sup> minute of cold application			
	≤ 15 °C	> 15°C	Total	
YOUNG group	76 (60.8%)	49 (39.2%)	125	
OLD group #	38 (30.4%)	87 (69.6%)	125	

# Statistical testing by Chi-Square test, P < .05

This result showed that the efficacy of cold application to skin temperature at  $15^{\circ}$ C cut off point was observed at a significantly greater frequency in YOUNG group more than OLD group (Table 4.5). However, different mean skin temperatures were not significant between YOUNG and OLD individuals for groups with skin temperature higher or lower than  $15^{\circ}$ C (Table 4.6).

 Table 4.6 Mean skin temperature responses at 20<sup>th</sup> minute of cold application in YOUNG and OLD groups

Group $\leq 15 ^{\circ}C$		> 15°C		
Group	Skin temperature ( <sup>°</sup> C)	p-value	Skin temperature ( <sup>o</sup> C)	p-value
YOUNG group	13.47 ± 1.36	0.151	17.81 ± 2.04	0.546
OLD group	13.79 ± 0.98	0.131	17.58 ± 2.17	0.040

# จุฬาลงกรณมหาวทยาลย

The relationship between leg skin temperature reduction and the decrement of lower – leg blood flow

Figure 4.6 and Figure 4.7 represented the overall relationship between absolute change of lower – leg skin temperature and blood flow reduction in YOUNG and OLD men.

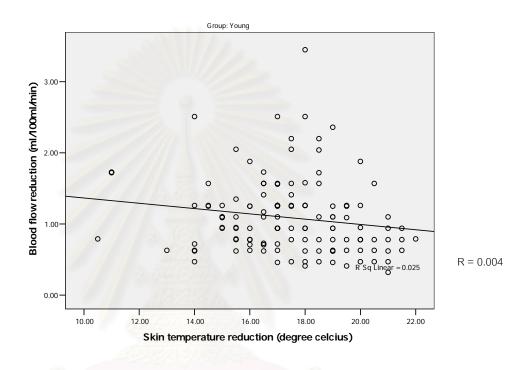


Fig 4.6 Correlation between lower – leg skin temperature and blood flow reduction in YOUNG men.

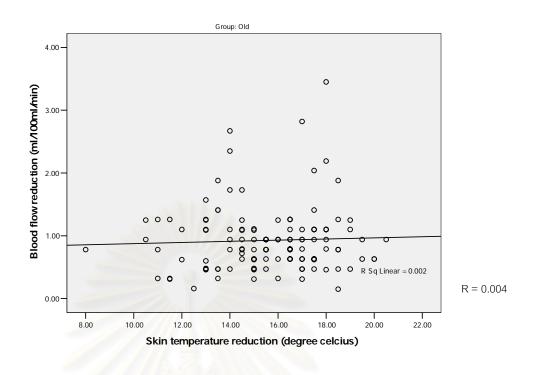


Fig 4.7 Correlation between lower – leg skin temperature and blood flow reduction in OLD men.

The result noted that the strength of the relationship between skin temperature reduction and the decrement of lower – leg blood flow was weak in YOUNG group (r=0.004) and OLD group (r=0.004).

### CHAPTER V

# DISCUSSION AND CONCLUSION

This study rigorously examined the lower – leg blood flow and skin temperature responses to cold application of two different subject groups. Both YOUNG and OLD groups showed significant reductions overtime in lower leg blood flow and skin temperature. The only significant difference between the two groups was that the YOUNG group had more reduction in skin temperature response to cold application by the end of the period.

#### Lower – leg blood flow responses to cold application

The results of this study included two important findings. First, the application of a cold pack to the lower - leg for a therapeutically accepted time period of 20 minutes (Cameron, 1999) and at a skin temperature of 10°C – 15°C (Rivenburgh. 1992) produced an immediate and continuous reduction in lower - leg blood flow. Several studies (Barcroft and Edholm, 1946; Clarke et al., 1957) have been conducted to measure blood flow during cold application in young men, where as none have been performed to measure blood flow responses to cold application in middle aged to elderly subjects. Furthermore, several other studies (Ho and Coel, 1994; Ho and Illgen, 1995; Karunakara and Lephart, 1999; Taber et al., 1992) have been conducted to examine the effects of other cold therapies on localized blood flow. These studies examined blood flow during cold gel pack or ice bag treatments by using various application durations. All of the studies consistently revealed a decreased blood flow at 20 minutes after application. Three of these studies (Karunakara, Taber, and Contryman) used an impedance plethysmograph to measure blood flow; whereas 2 others (Ho and Illgen) used triple-phase technetium bone scans to measure blood flow. It should also be noted that several of the studies were conducted more than 40 years ago (Barcroft, 1946; Clarke, 1958; Lewis and Grant, 1925). Although there were different methods in examining the physiological response to cold application, the results also showed a decreased in blood flow that was supported by this study. Interestingly, the cold application did not have to be continuously applied to cause a blood flow reduction as

Karunakara et al (1999) reported a decrease in local blood flow with a prolonged (60 minutes) intermittent cold application.

The result from this study indicated the absolute significant blood flow reduction in both YOUNG and OLD groups when compared with resting blood flow. As local tissue was not traumatized and no significant change in the subject's heart rate or blood pressure was observed it may be concluded that the reduced blood flow during cold application was likely attributable to constriction of the local vasculature (Taber, 1992)

The second important finding was that the difference in lower – leg blood flow reduction was not observed between YOUNG and OLD groups during the 20 – minute of application. During cold application, blood flow to the leg was lower in OLD subjects compared to YOUNG subjects; this maybe resulted from peripheral (reduced leg vascular conductance) limitations (Wagner et al., 1974). There is considerable variability in the literature concerning age – related changes in peripheral circulation in the cold. Under a mild exposure to cold air (17°C), older subjects reduced finger blood flow less than younger subjects (Wagner et al., 1974). Years later the same group (Wagner JA, Horvath SM; 1985) obtained similar results on forearm blood flow when the cold exposure was more severe (2 hours at 10°C). Collins et al (1997) did a longitudinal study on subjects (69 years or older), in which measurement hand blood flow responses to cold were monitored. Before the follow – up 37 out of 43 subjects exhibited a vasoconstrictor response to cold, but after 4 years only 29 had maintained their vasoconstrictor response.

Not only did the leg blood flow decrease immediately and rapidly after cold application and continue to decrease gradually for the duration of the application, but the changes were also not different between groups at the end of the application. So, applying the ice pack at the ankle for 20 minutes did not support theory of the vascular dysfunction especially in the middle aged to elderly subjects. Moreover, in this study, cold – induced reactive vasodilation was not observed over the course of cold application for both groups. It is possible that vasodilation may occur after the removal of the ice pack. However, blood flow data following removal of the cold application was not obtained as part of this study. Additional work is needed to clarify the local vascular response, if any, following ice pack removal. In addition, investigating the proximal and distal spread of cold temperature in deeper tissue, further investigations using invasive techniques are of great interest. In addition, the redness of skin at lower – leg was observed with associated symptoms such as numbness. The redness of skin was explained by 2 theories, the first theory is that cold application causes a greater decrease in venous return than in arterial inflow, resulting in arterial hyperemia in the skin (Licht, 1982). The second theory is that tissue metabolism decreases during cold application, and oxygen exchange between the tissues and capillaries also decrease, resulting in more highly oxygenated blood in the skin's venous system (Greenfield, 1963).

### Lower – leg skin temperature responses to cold application

This study investigated the response of a 20 – minute application of cold pack on the lower – leg skin temperature. The results suggested that both groups illustrated a similar pattern of skin temperature reduction, in which a sharp fall occurred within the first few minutes after the application and had decreased gradually over the application time. The rapid decrease in the lower – leg skin temperature observed during the first few minutes and the slow and steady decline for the duration of the cold application found in the present study were in agreement with others (Bugas, 1975; Myncuso, 1986; Petajon, 1962; Dost, 1990).

When comparing the skin temperature changes in the YOUNG and OLD subjects, the current study found that the YOUNG subjects experienced greater mean skin temperature changes than the OLD subjects. The differences in skin temperature during cold application between YOUNG and OLD group were statistically significant at baseline and the 20<sup>th</sup> minutes of application.

Changes in skin temperature under cold application may indirectly indicate the degree of skin vasoconstriction (Wagner and Robinson, 1974). For the elderly, there also seemed to be a diminished capacity of autonomic reflexes that control blood flow. At rest, circulation to the skin was often poor, which could make peripheral body parts uncomfortably cold (Brooks and Fashey, 1988). Thus, an older limb with diminished arterial blood flow would be cool to the touch. However, human aging substantially impairs cutaneous vasoconstriction (Khan et al., 1992; Richardson et al., 1992; Kenney and Armstrong, 1996; Thompson and Kenney, 2004), rendering older people more susceptible to excessive heat loss and potentially hypothermia (Collins et al., 1977; Budd et al., 1991; Inoue et al., 1992). While several thermoregulatory studies have addressed age - related changes in reflex - mediated vasoconstriction, it is unclear whether this blunted vasoconstriction response in aged skin is likewise seen with local cooling, which involves different downstream mechanisms. Very little was known regarding how local cooling affects vasoconstriction in aged human skin. Although there was presently little data addressing the effects of advancing age on the mechanism of local cooling, this study originally hypothesized that the OLD subjects had different in response to local cooling compared with the YOUNG subjects. Healthy aging is generally associated with impaired cutaneous vasomotor function, including blunted reflex vasoconstriction and vasodilatation as well as attenuated vasodilatation in response to local heating (Kenney and Armstrong, 1996; Kenney et al., 1997; Minson et al., 2002; Pierzga et al., 2003; Thompson and Kenney, 2004). Therefore, the present study supported the previous evidence by demonstrating that the response of skin temperature to local cooling changes with age.

#### The relationship between skin temperature reduction and leg blood flow

Skin temperature often is used as an index of blood flow in the extremities; even though the relation may be merely implicit (Fetcher et al., 1946). Lewis (1936) mentioned that skin temperature is valid as a measure of extremity blood flow only under certain conditions. Skin temperature depends upon both the rate of heat supply to the skin and the rate of heat removal that is, upon the temperature and flow

rate of the blood, and the insulation and temperature difference between skin and environment. If the temperature difference is small, heat will be removed so slowly that even large changes of blood flow will have little effect on the skin temperature (Lewis, 1936).

The attempt of this study attempting to correlate skin temperature reduction to lower-leg blood flow reduction presented conflicting results. Intuitively, we would expect to see a direct relationship between a skin temperature reduction and blood flow decrease during cold application. When skin temperature gets cooler, we would expect to see more blood flow reduction. A lack of relationship was found between absolute decreases of skin temperature and lower – leg blood flow reduction in both YOUNG and OLD group suggested that skin temperature may have little effect on blood flow response.

In contrast, Rubinstein and Sessler (1990) compared the steady – state skin temperature gradients with total fingertip blood flow in 19 healthy volunteers. There was an excellent correlation between steady – state skin temperature gradients and total fingertip blood flow measured with venous – occlusion plethysmography (r = 0.98). The authors conclude that skin temperature gradient is an accurate measure of thermoregulatory peripheral vasoconstriction.

Generalization of the results from this study to a clinical practice is limited by several factors that might have influenced the absolute amount of skin temperature reduction. The first is that the mean skin temperature of injured condition is commonly higher than that of noninjured condition. The higher mean skin temperature would have been expected if the temperature of the application area was higher. The second is that the temperature of the damp towel wrapped around the modalities was at room temperature. The lower skin temperature reduction would have been observed if the temperature of damp towel were higher. The third factor is that the subjects' skinfold thickness, which was controlled to be not greater than 40 mm (Kenny and Humphrey, 1995). Likewise, the mean skin temperature reduction would have been higher in subjects with lower skinfold thickness because a large amount of heat could be transferred from the underlying muscle to the skin surface and the cryotherapy modalities. Older people whose skinfold thickness is relatively higher than that of younger would therefore, demonstrate higher mean skin temperature during cryotherapy. The fourth factor is the environmental temperature, which was controlled at a specified level. The deviation in ambient temperature from this study could have led to differences in absolute mean skin surface temperature. Another factor is that the size and weight of the cryotherapy modalities used in this study was controlled. Differences in these characteristics may affect to which skin surface temperature and blood flow is reduced.

# Conclusion

Young men were superior to the middle aged to elderly men in reducing skin temperature to fall to the levels required for therapeutic effects. However, leg blood flow response to cold application was similar in the young and middle aged to elderly individuals.

Moreover, the reduction in lower – leg blood flow was non – coincided a reduction in skin temperature when ice pack was applied to the ankle for a period of up to 20 minutes. Thus, it is suggested that middle aged to elderly men had less effective local skin temperature control while their leg blood flow response to cold was intacted.

#### REFERENCES

Anderson MK, Hall SJ. <u>Sports injury management</u>. Williams & Wilkins, Media PA, 1995. Baker RJ and Bell GW. The effect of therapeutic modalities on flow in the human calf.

<u>J Orthop Sports Phys Ther</u> 13 (1991): 27 – 37.

- Brooks GA and Fashey TD. <u>Exercise physiology: Human bioenergetics and its</u> <u>applications</u> Human kinetics, 1988.
- Bugaj R. The cooling, analgesic and rewarming effects of ice massage on localized skin. <u>Phys Ther</u> 55 (1975) : 11 19.
- Cameron MH. <u>Physical agents in rehabilitation: from research to practice</u> Philadelphia: WB Saunders, 1999.
- Chesterton LS, Foster NE, Ross L. Skin temperature response to cryotherapy. <u>Arch Phys</u> <u>Med Rehabil</u> 83 (2002): 543 – 549.
- Cohn BT, Draeger RI, Jackson DW. The effects of cold therapy in the postoperative management of pain in patients yndergoing anterior cruciate ligament reconstruction. <u>Am J Sports Med</u> 17 (1989): 344 349.
- Cote DJ, Prentice WE, Hooker DN et al. Comparison of three treatment procedures for minimizing ankle sprain swelling. <u>Phys Ther</u> 68 (1988): 1064 1076.
- Deal DN, Tipton J, Rosencrane E, Curl WW, Smith TL. Ice reduces edema. <u>J Bone Joint</u> Surg Am 84 (2002): 1573 – 1578.
- Edwards DJ, Rimmer M, Kenne GC. The use of cold therapy in the post operative management of patients undergoing arthroscopic anterior cruciate ligament reconstruction. <u>Am J Sports Med</u> 24 (1996): 193 195.
- Evans P. <u>The healing processes at cellular level: A review physiotherapy</u> 66 (1980): 256 – 259.
- Felsenthal G, Garrison SJ, Steinberg FU. <u>Rehabilitation of the aging and elderly patient</u> Baltimore: Williams & Wilkins, 1994.
- Ficus KA, Kaminski TW, and Powers ME. Changes in lower-leg blood flow during warm-, cold-, and contrast – water therapy. <u>Arch Phys Med Rehabil</u> 86 (2005): 1404 – 1410.

- Groothuis JT, Vliet LV, Kooijman M and Hopman MT. Venous cuff pressures from 30 mmHg to diastolic pressure are recommended to measure arterial inflow by plethysmography. <u>J Appl Physiol</u> 95 (2003): 342 347.
- Hill JW, Petrucci RH. <u>General chemistry: an integrated approach</u>. 3<sup>rd</sup> ed. Upper Saddle River: Prentice – Hall, 2002.
- Hochberg J. A randomized prospective study to assess the efficacy of two cold therapy treatments following carpal tunnel release. <u>J Hand Ther</u> 14 (2001): 208 215.
- Hokanson DE, Sumner DS, Strandness DE. An electrically calibrated plethysmograph for direct measurement of limb blood flow. <u>IEEE Trans Biomed Eng</u> (1975); 22: 25 – 29.
- Holcomb WR, Mangus BC, Tandy R. The effect of icing with the pro-stim edema management system on cutaneous cooling. <u>J Athletic Train (Dallas</u>) 31 (1996): 126 129.
- Hubbard JT, Stephanie LA, Craig RD. Does cryotherapy hasten return to participation? A systematic review. <u>J Athletic Train (Dallas)</u> 39 (2004): 88 – 94.
- Johannsen F, Langberg H. The treatment of acute soft tissue trauma in Danish emergency rooms. <u>Scand J Med Sci Sports</u> 7 (1997): 178 – 181.
- Jutte LS, Merrick MA, Ingersoll CD, Edwards IE. The relationship between intramuscular temperature, skin temperature and adipose thickness during cryotherapy and rewarming. <u>Arch Phys Med Rehabil</u> 82 (2001): 845 850.
- Kallinen M and Markku A. Aging, physical activity and sports injuries: An overview of common sports injuries in the elderly. <u>Sports Med</u> 20 (1995): 41 52.
- Kellnet J. Acute soft tissue injuries: A review of the literature. <u>Med Sci Sports Exerc</u> 18 (1986): 489 500.
- Kenneth KL. <u>Cryotherapy in sports injury management</u>. Champaign: Human kinetics, 1995.
- Kerr KM, Daily L, Booth L. <u>Guidelines for the management of soft tissue</u> (musculoskeletal) injury with protection, rest, ice, compression, and elevation (PRICE) during the first 64 hours London, Chartered Society of Physiotherapy, 1999.

- Knight KL. Effects of hypothermia on inflammation and swelling. <u>J Athletic Train</u> 11 (1976): 7 10.
- Knight KL, Brucker JB, Stoneman PD et al. Muscle injury management with cryotherapy. <u>Athletic Therapy Today</u> 5 (2000): 26 – 30.
- Laba E. Clinical evaluation of ice therapy for acute ankle sprain injuries. <u>NZ J Physiother</u> 17 (1989): 7 – 9.
- LaVelle BE and Snyder M. Differential conduction of cold through barriers. <u>J Adv Nur</u> 10 (1985): 55 61.

Lee JM, Warren MP, Mason SM. Effects of ice on nerve conduction velocity.

<u>Physiotherapy</u> 64 (1978): 2 – 6.

- Lephart SM, Karunakara RG, Pincivero DM. Changes in forearm blood flow during single and intermittent cold application. <u>J Orthop Sports Phys Ther</u> 29 (1999): 177 – 180.
- Levy AS, Kelly B, Lintner S et al. Penetration of cryotherapy in treatment after shoulder arthroscopy. <u>Arthroscopy</u> 13 (1997): 461 464.
- MacAuley D. Ice Therapy: How good is the evidence? Int J Sports Med 22 (2001): 379 – 384.
- MacAuley D. Do textbooks agree on their advice on ice? <u>Clin J Sport Med</u> 11(2001): 67 – 72.
- Malone TR and Kirpatrick JS. Nerve injury in athletes caused by cryotherapy. <u>J Athletic</u> <u>Train (Dallas)</u> 27 (1992): 235 – 237.
- McMeeken J, Murray L, Cocks S. Effects of cooling with simulated ice on skin temperature and nerve conduction velocity. <u>Aust J Phys</u> 30 (1984): 111 – 114.
- Meeusen R, Lievens P. The use of cryotherapy in sports injuries. <u>Sports Med</u> 3 (1986): 398 414.
- Merrick MA, Rankin JM, Andres FA, Hinman CL. A preliminary examination of cryotherapy and secondary injury in skeletal muscle. <u>Med Sci Sports Exerc</u> 31 (1999): 1516 – 1521.
- Merrick MA. Secondary injury after musculoskeletal trauma: A review and update.

<u>J Athletic Train</u>. 37 (2002): 209 – 217.

- Michlovitz S, Smith W, Watkins M. Ice and high voltage pulsed stimulation in treatment of acute lateral ankle sprains. <u>J Orthop Sports Phys Ther</u> 9 (1988): 301 304.
- Moeller JL, Monroe J, McKeag DB. Cryotherapy induced common peroneal nerve palsy. <u>Clin J Sport Med</u> 7 (1997): 212 216.
- Myrer JW, Measom G, Fellingham GW. Temperature changes in the human leg during and after two methods of cryotherapy. <u>J Athl Train</u> 33 (1998): 25 – 29.
- Ohkoshi Y, Ohkoshi M, Nagasaki S, Ono A, Hashimoto T, Yamane S. The effect of cryotherapy on intraarticular temperature and postoperative care after anterior cruciate ligament reconstruction. <u>Am J Sports Med</u> 27 (1999): 357 – 362.
- Otte JW, Merrick MA, Ingersoll CD, Cordova M. Subcutaneous adipose tissue thickness alters cooling time during cryotherapy. <u>Arch Phys Med Rehabil</u> 83 (2002): 1501 1505.
- O'Toole G and Rayatt S. Frostbite at the gym: A case report of an ice pack burn. <u>Br J</u> <u>Sports Med</u> 33 (1999): 278 – 279.

Prentice WE, Arnheim DD. Principles of athletic training. 10<sup>th</sup> ed. McGraw-Hill, 2000.

- Rivenburgh DW. Physical modalities in the treatment of tendon injuries. <u>Clin Sports Med</u> 11 (1992): 645 – 659.
- Robergs RA and Roberts SO. <u>Exercise</u>, <u>performance</u>, <u>and clinical applications</u>. McGraw-Hill, 1997.
- Rooke GA, Savage MV, Brengelmann GL. Maximal skin blood flow is decreased in elderly men. J Appl Physiol 77 (1994):11 14.
- Sapega AA, Heppenstall B, Sokolow DP et al. The bioenergetics of preservation of limbs before replantation. <u>J Bone and Joint Surg</u> 70A (1988): 1500 1513.
- Sloan JP, Hain R, Pownall R. Clinical benefits of early cold therapy in accident and emergency following ankle sprain. <u>Arch Emerg Med</u> 6 (1989): 1 6.

Sports injuries rising in the elderly. <u>BMJ</u> 323 (2001): 328 – 331.

- Swensen C, Sward L, Kartsson J. Cryotherapy in sports medicine. <u>Scand J Med Sci</u> <u>Sports</u> 6 (1996): 193 – 200.
- O'Toole G and Rayatt S. Frostbite at the gym: A case report of an ice pack burn. <u>Br J</u> <u>Sports Med 33</u> (1999): 278 – 279.

- Taber C, Contryman K, Fahrenbruch J, LaCount K, Cornwall M. Measurement of reactive vasodilation during cold gel pack application to nontraumatized ankles. <u>Phys</u> <u>Ther</u> 72 (1992): 294 – 299.
- Thorsson O. Cold therapy of athletic injuries: A literature review. <u>Lakartidningen</u> 98 (2001): 1512 1513.
- Weston M, Taber C, Cornwall M, Casagranda L. Changes in local blood volume during cold gel pack application to traumatized ankles. <u>J Orthop Sports Phys Ther</u> 4 (1994): 197 199.
- Wilson JD, Isselbacher KJ, Braunwald E, Martin JB, Fauci AS and Kasper DL. <u>Harrison's</u> principles of internal medicine 13<sup>th</sup> ed. McGraw-Hill, 2000.
- Zachariassen KE. Hypothermia and cellular physiology. <u>Arctic Med Res</u> 50 Suppl (1991): 13 17.
- Zemke JE, Anderson JC, Guion WM et al. Intramuscular temperature responses in the human leg to two forms of cryotherapy: ice massage and ice bag. <u>J Orthop</u> <u>Sports Phys Ther</u> 27 (1998): 301 – 307.

# BIOGRAPHY

Miss Saowapa Thumapun was born on 12 July 1980. She graduated a Bachelor of Science in Physiotherapy from the Faculty of Allied Health Sciences Chulalongkorn University in 2001.

She had been working as a physiotherapist at Nakornthon Hospital from July 2001 to June 2002 and worked as a personal trainer at California Fitness Center from July 2002 to December 2003.

