Nova Southeastern University
Institutional Review Board for Research with Human Subjects (IRB)
New Protocol Submission

Center Rep:	**To be completed by IRB Office**
Date Sent to IRB:	**Protocol Number:**

Instructions: In order to comply with federal regulations and with the university's IRB guidelines, the Principal Investigator (PI) is required to complete all of the following items. After completing, submit this document and all consent forms and research instruments (questionnaires, interviews, etc.) to the appropriate IRB College/Center Representative. You can find your college/center representatives using the following link: http://www.nova.edu/irb/membership.html.

- If your study qualifies for center level exemption from further review, the Center Representative will exempt your study, provide you with a memo to that regard, and give you copies of the stamped, approved consent/assent form(s), if applicable. The Center Representative will log your study into the IRB database and forward a copy of the complete submission to the IRB office.
- If your study appears to qualify for expedited review, then once the Center Representative believes the submission is complete, the Center Representative will log your study into the IRB database and forward ONE complete submission packet to the IRB office for review.
- If full review is required, the Center Representative will log the study into the IRB database and will provide the PI with instructions for submitting 2 stapled or rubber banded copies (AND 1 unstapled original) of the submission and all supporting materials (research protocol, consent/assent forms, letters of authorization, etc.) to IRB. Please note: ONLY ONE copy of all research instruments (tests instruments, interview protocols, etc.) needs to be submitted. The completed package must be received by the IRB by the last business day of the month prior to the next scheduled IRB meeting. Because mail, including express delivery, takes at least a day to be delivered within the university, please make allowance for this in your planning. Incomplete submissions will delay review by the IRB. The IRB reserves the right to postpone review of protocols at convened meetings due to needed revisions.

Use a word processor to complete this form. You do not need to be concerned about where page breaks fall. You are to complete all BLUE sections. Be sure that all pages, including any appendices or attachments, except for consent/assent forms and advertisements, are numbered sequentially. For further information, refer to http://www.nova.edu/irb/manual/policies.html and http://www.nova.edu/irb/process.html

Do not approach subjects about being in the research study until you have received NSU IRB approval.

Form Version: August 1, 2013

1. General Information

1.A. Research Project Title:

Effects of Heat-Induced Skin Blood Flow Changes on Skin Water Parameters

1.B. Insert Principal Investigator's (PI) Last Name and Date of Submission in the footer.

1.C. Brief Overview (Max 250 Words):

Skin heating is associated with skin blood vessel vasodilation and increased skin blood flow. We hypothesize that such vasodilation should be associated with an increase in the amount of fluid filtered from the capillaries distal to the arteriolar vasodilation and that the subsequent increase in interstitial fluid is dependent on the amount of the blood flow increase. To test this hypothesis we plan to locally heat the skin, measure the blood flow produced and noninvasively measure parameters to assess the skin water changes. These measurements are: 1) tissue dielectric constant (TDC) which assesses the skin-to-fat water content, 2) stratum corneum (SC) electrical capacitance which assesses SC water content and 3) transepidermal water loss (TEWL) that assesses water loss from the skin. Measurements will be done in both sexes (35 male and 35 female with age-range of 18-35 years) since the literature indicates gender differences in skin blood flow and skin water content. Skin heating will be produced by a topically applied 20 mm disk that will cause skin to be heated to 40°C for 12 minutes. Blood flow during this time is monitored via a laser Doppler method. The target measurement site is the dominant anterior forearm 6 cm distal to the antecubital crease. Tissue water parameters will be measured prior to heating, immediately after heat removal and at 2-minute intervals for 12-minutes post-heating. The protocol, including initial set-up, subject acclimation and measurements will take about 45 minutes. The hypothesized dependence of tissue water on induced blood flow will be tested by regression analysis. Gender differences in measured parameters will be tested with independent T-tests with a p-value <0.05 accepted as significant.

1.D. Principal Investigator (PI) Information

Name	Harvey N. Mayrovitz PhD	Relationship to NSU	
Mailing Address (for Students)			
Interoffice Mail Code (for Faculty/Staff)	3200 S. University Drive, Davie, FL 33328	Student	
Daytime Phone	954-262-1313	Faculty	X
Alternate Phone		Staff	
NSU Email Address	mayrovit@nova.edu	NSU Center/College/Dept	
Alternate Email Address		HPD/CMS/PHYSIOLOGY	
Degree/Academic Information		PI CITI Completion Date*	
		09/09/2014	

Please briefly describe your applicable professional, educational, employment, professional licensure, and research experience. Do NOT attach your vitae.

PhD, 20 years of research experience.

1.E. Co-Investigators (Co-I) Information (including faculty advisers)

	Co-Investigator 1	Co-Investigator 2	Co-Investigator 3
Name	Shalaka Akolkar	Anita Singh	Foster Scott Lerner
Mailing Address	2640 S. University Dr. #222	3001 W. Rolling Hills Circle. #205	2600 S. University Dr. #317

	Davie, FL 33328	Davie, FL 33328	Davie, FL 33328
Contact Phone Number	734-223-3044	954-803-6970	850-629-0487
Email Address	sa1223@nova.edu	as1438@nova.edu	fl222@nova.edu
Degree/Academic Information:	2nd year osteopathic medical student	1st year osteopathic medical student	M.A., 2nd year osteopathic medical student
CITI Completion Date*	08/06/2014	9/8/2014	03/11/2014

Please briefly describe applicable professional, educational, employment, professional licensure, and/or research experience for all co-investigators. Do NOT attach vitae.

Lerner – B.S. in Biology, M.A. in Biology, 2 years of research experience.
Singh –B.S. in Biology, 1 year of research experience.
Akolkar –B.S. in Psychology, 3 years of research experience.

1.F. Research Assistant Information (if applicable)

	Research Assistant 1	Research Assistant 2	Research Assistant 3
Name			
Mailing Address			
Phone Number			
Email Address			
CITI Completion Date*			

*NOTE: CITI must have been completed within the last 3 years. If a member of the research team is affiliated with another institution, please include a copy of that individual's training certification.

1.G. Funding Information

Funding status	Unfunded	Funding Applied For	Funded
	X		

If you indicated "Funded" or "Funding Applied For," complete the following.

Source of Funding				
Project Title (if different from above)				
Principal Investigator (if different from above)				
Type of Application	Grant	Subcontract	Contract	Fellowship
Award Amount:				

1.H. Management of Conflict of Interest

Read the financial conflict of interest policy at http://www.nova.edu/irb/manual/forms/significant-financial-interest.pdf

I certify that I, as PI, have read this policy, and have verified that my co-investigators and research assistants also have read this policy.

PI Initials	HNM

For studies that are funded by a governmental agency (any federal, state or local governmental entity that has promulgated regulations or policies requiring investigator financial disclosure or requiring institutional conflict of interest policies relating to award of grants or contracts) read the Office of Sponsored Program's Financial Conflicts of Interest in Sponsored Programs policy.

I certify that I, as PI, have read these guidelines, and have verified that my co-investigators and research assistants also have read these guidelines.

PI Initials	HNM

Do any investigators have a significant financial interest, as defined in the above referenced policy, in relation to this study?

Yes	No
	X

If yes, please describe the nature of the conflict of interest below

If you answered yes, please be sure to include the following statement, or a similar statement, within the description section of the consent forms: "The principal investigator and/or co-investigator(s) of this research study have a significant financial interest as it relates to this study." Continue, describing the conflict in the consent/assent documents.

1.I. Dates and Phases of Study

Proposed Start Date			
Shortly after IRB approval	X	Other (list date)	

Proposed Duration of Research (including analysis of the results)	
One year or less X	Other (describe, please note minimum annual continuing review required)

Is this a multi-part study?

Yes	No
	X

If "Yes," please note that procedures used in later phases may affect the review status of this study. Briefly describe the later stages.

1.J. Multiple Site Information

Will the study be conducted at an NSU location?

Yes	No
X	

If "Yes," provide the location within NSU, e.g. department or clinic.

Terry Building, Third Floor, Room 1305A

College of Medical Sciences/HPD

Will the study involve any NSU faculty, staff or students as subjects?

Yes	No
X	

Will the study be conducted at a non-NSU location?

Yes	No
	X

Will any of the activities be done online or via telephone (e.g., completion of surveys, delivery of instructional content)?

Yes	No
	X

If "Yes", for the Internet based activities, will these be done via a secure site?

Yes	No

If "Yes," please complete the following for the non-NSU sites.
Include these sites on the consent form in the "site information" section.

	Site 1	Site 2	Site 3
Site Name			
Address			
Phone Number			

You will need documentation of permission to conduct the research at non-NSU sites. Attach the permission letter(s) or IRB approvals to this document.

1.K. Cooperative Research

Cooperative research projects are those that involve more than one institution or when an investigator is employed at or is an agent of an institution other than NSU, (For more information, see http://www.hhs.gov/ohrp/humansubjects/guidance/engage08.html). Each participating institution is responsible for safeguarding the rights and welfare of human subjects and for complying with all regulations.

Does this research involve cooperative research?

Yes	No
	X

Has this proposal been submitted or will the proposal be submitted to another Institutional Review Board (or authorizing individual, entity, or ethics review board) for review?

Yes	No
	X

If "Yes," please complete for each site. Please attach documentation of approval.
(Copy the section of the table and add if there are multiple sites.)

Name of Institution	

IRB/Administrative Decision (check applicable)			
Approved	Submitted	Not yet submitted	NSU IRB approval required prior to

	(not yet approved)		submission

Date of Review	Contact Person Phone Number	Level of Review (if IRB Reviewed)		
		Exempt	Expedited	Full

2. Subject/Participant Information

2.A. Overview of Proposed Subjects/Participants
(complete all that apply and provide maximum number proposed within each category):

Subject Group	Fetus in Utero/ non-viable fetuses/ abortuses	Newborns or Infants	Children (aged 2-6)	Children (age 7-12)	Adolescents (aged 13-17)	Adults (18+)	Pregnant Women	Adults with Guardians
Mark X for each proposed subject type						X		
# of Proposed Subjects*						70		

Please briefly describe your potential subjects:

Self-reported healthy adults with ages between 18 - 35 years; half male and half female.

*By proposed subjects, the IRB means subjects who will consent to be in the study and begin the study activities.

2.B. Subject Vulnerability

Do any subjects have limited decision-making autonomy, have communication problems that would limit ability to dissent to study procedures, belong to a group that is vulnerable to coercion, or belong to a group defined by regulation as requiring greater care?

Yes	No
x	

If you indicated "Yes", please mark with an X next to each applicable category in the column to the right and complete the remainder of this section

Prisoners	
Pregnant Women	
Cognitive impairment or emotional problems that potentially limit decision making	
Communication impairments that may preclude communicating a decision to discontinue participation or refuse participation	
Students of the investigator or investigator's department	x
Employees of the investigator or investigator's department	
Children (minors)	
Terminally ill	

Other (specify):

If you indicated any of the above, please justify your rationale for including these subjects.

The study is open to all subjects who are self reported healthy. Some of these may be Dr. Mayrovitz's students. Participation in the study is completely voluntary. Their decision on whether they will or will not participate in the study will not impact their course grade, if they are Dr. Mayrovitz's students.

If you are using potentially vulnerable subjects as described above (infants, children, pregnant women/fetuses, terminally ill, decision-impaired, communication-impaired, students/employees, or prisoners), does the research create greater than minimal risk?

Yes	No
☐	☐

If your subjects have a vulnerability that arises from their being students in your class or department, you will be asked for more information in Section 3.G. If the subjects have one of the other vulnerabilities, please describe proposed safeguards to protect vulnerable subjects.

If not evident from the researcher qualification information in 1.D. or 1.E., please describe the researcher(s) qualifications for working with vulnerable subjects

2.C. Study Design and Methodology

Part 1 – Purpose

Please briefly describe the purpose of your study. Note: Examples of study purposes are "to determine if a new reading intervention program improves 4th graders' reading scores" or "to survey patients on their perception of physical therapy services".

Skin heating is associated with skin blood vessel vasodilation and increased skin blood flow. We hypothesize that such vasodilation should be associated with an increase in the amount of fluid filtered from the capillaries distal to the arteriolar vasodilation and that the subsequent increase in interstitial fluid is dependent on the amount of the blood flow increase. Our purpose is to test this hypothesis since the process being investigated impacts our basic understanding of skin-related physiology and has potential extensions to skin-related clinical issues.

Part 2 – Goals and Justification

Briefly elaborate on the main goals and justification for the study. Summarize the background, rationale, nature, and significance of the proposed research. Include a brief overview of your prior research in the area, or literature that supports the need for this study. This section should be a brief overview, and typically is not more than a few paragraphs in length. You will be asked about procedures and instruments later in the submission.

Prior research[1] has investigated the relationship between skin heat-induced vasodilation and the sympathetic nervous system. It was found that despite chemically induced nerve conduction blocks to the axons of the sympathetic nerves supplying forearm skin, local heating continued to produce a

vasodilation effect. This showed that withdrawal of sympathetic tone was only one mechanism involved. Other work has demonstrated that are in fact at least two mechanisms contributing to the rise in skin blood flow during non-painful heating; a fast responding vasodilation mediated by the axon reflexes and a slower response relying on the production of nitric oxide (NO).[2] This dual mechanism became evident in experiments in which the action potential conduction of the axon was blocked using an EMLA cream and NO synthase (NOS) inhibition was achieved with L-NAME. It was shown that the role of NO was about 1.75 times greater than the role of the sympathetics. Further examining the sympathetic response aspect of this theory, Charkoudien et al[3] found that despite undergoing a complete regional sympathectomy for treatment of palmar hyperhidrosis, patients continued to display substantial heat-induced vasodilation. Furthermore, it has been found that NO is involved in sustaining the hyperemic response after heating, such that removal of NO by L-NAME causes a faster fall in blood flow after 30 minutes post heating.[4] Because NO is involved with changes in vascular permeability as well as vasodilation we believe that there is a direct relationship between the amount of tissue water leaked into the interstitium and the amount of blood flow caused by local heating. Specifically, we hypothesize that skin blood vessel vasodilation should be associated with an increase in the amount of fluid filtered from the capillaries distal to the arteriolar vasodilation and that the subsequent increase in interstitial fluid is dependent on the amount of the blood flow increase. Because this is a fundamental physiological process that is not well understood it is our goal to investigate this issue and to test the working hypothesis. Because other research has shown that gender differences exist in the NO activity[4], blood flow and skin water, it is important to study these issues in both genders as is presently planned.

Part 3 – Steps in the Research Study

In the box below, please outline in detail the steps in the research study in order as they will occur after consent has been secured. If there are different requirements for different groups/types of subjects within the study, please separate out the steps per group. Indicate how long the subject spends completing the different steps/procedures. Be specific about the tests given and/or treatments used, when they will occur, and their frequency.

METHODS:

A. Subjects:

A total of 70 subjects will be recruited for participation in this research study. It is planned to have 35 males and 35 females between the ages of 18 and 35 who will be evaluated according to the protocol subsequently described. Recruitment of subjects will be done by the co-investigators who will advertise by word of mouth within the University and by use of a flier (Appendix 1) to recruit volunteer subjects from University staff, faculty and students. The Co-investigators are conducting the study, after receiving training from the investigator Dr. Mayrovitz. It is planned to offer an honorarium in the form of a $10 gift card to subjects who participate in this approximately 45 minute, single-session research study. If a potential subject is interested in participating, they will meet with a co-investigator, who will explain the study in detail and administer the consent form. The research experimental measurements to be described will be done in the HPD Terry Building of Nova Southeastern University in room 1305A.

B. Measurement Methods, Procedures and Devices:

Overview: Skin blood flow will be measured via a laser Doppler method before, during and after local heating (section B4). Skin-to-fat water content will be measured before and after heating using the method of tissue dielectric constant (TDC) as described in section B1. Stratum corneum water will be measured using electrical capacitance methods (section B2) and skin water loss will be measured by the method of transepidermal water loss (section B3). Skin temperatures will be measured with a infrared non-contact thermometer

B1. Local Tissue Water via Tissue Dielectric Constant Method

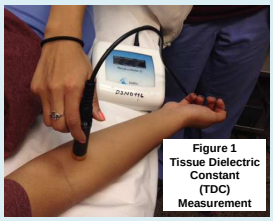

Figure 1 Tissue Dielectric Constant (TDC) Measurement

The method is based on the principle that the tissue dielectric constant (TDC) is directly related to the amount of free and bound water contained in the measuring volume[5-12]. The TDC of specific target areas is determined using a coaxial probe that makes contact with the skin for about 10 seconds. The probe, which is connected to a control and display device, measures the TDC at a frequency of 300 MHz. At this frequency the TDC is an index of both free and bound water. The penetration depth of the measurement depends on the probe size, with larger diameter probes penetrating deeper. The output parameter is the TDC value that has a range of 1 to 80. For reference, pure water has a value of about 78.5. For this study probes with effective penetration depths of about 1.5 and 2.5 mm will be used (Fig 1). These measurements will be made on dominant arm anterior forearm site. The device to be used is the battery operated Moisture MeterD (Delfin Technologies Ltd. Kuopio FINLAND).

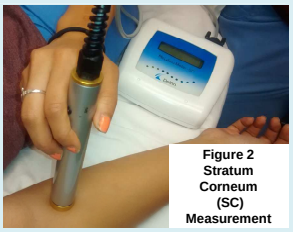

Figure 2 Stratum Corneum (SC) Measurement

B2. Method for Measurement of Stratum Corneum Hydration

The method is based on the principle that the measured electrical capacitance between the skin surface to a depth of about 100 um is an index of the relative water content of the stratum corneum (SC). The device to be used for this measurement in the present study is the hand held battery operated MoistureMeter SC also manufactured by Delfin Technologies Ltd and pictured adjacent. A measurement is taken by touching the skin surface with the end of the probe for about 10 seconds and the relative SC moisture is displayed on the device meter.

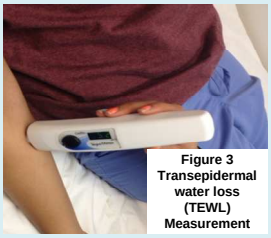

Figure 3 Transepidermal water loss (TEWL) Measurement

B3. Method for Measurement of Transepidermal Water Loss (TEWL)

The method is based on the principle that the water flux (ml/m^2/min) leaving skin can be quantified by collecting the effluent within a closed chamber and determining the change in relative humidity within the chamber. The device to be used for this purpose is the hand-held battery operated VapoMeter also manufactured by Delfin Technologies Ltd. The measurement procedure requires the touching of the skin with the tip of the device for about 10 seconds after which the TEWL value is automatically displayed.

B4. Method for Measuring Skin Blood Flow Non-Invasively

Skin blood flow (SBF) will be measured by a laser-Doppler flowmetry system (Vasamedics BPM2, Blood Perfusion Monitor). With this method the flux of red blood cells is detected by a small sensor taped to the skin. The sensor transmits a very low level laser light and also recovers the reflected signal that has a change in wavelength proportional to skin blood flow. The sensor is connected to a laser-Doppler monitoring and processing device via a fiber optic lead that converts the signal to blood perfusion units. This measurement method is in standard use clinically and for research purposes and its use for various purposes has been documented in over a thousand published papers. The principal Investigator has used this technique for over fifteen years and the device is FDA 510K registered. The fiberoptic probe is inserted directly through the concentric heating element and taped to the skin as shown in Figure 4.

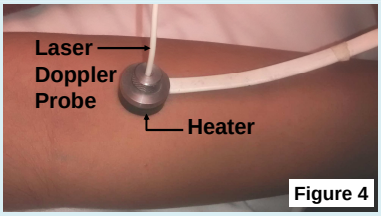

Figure 4

C. Protocol:

Set-up

After explaining the study and having the consent form signed, the subject will be asked if they wish to use the restroom before the study begins. Next, the subject will be asked to lie supine on an examination table and a light blanket will be draped across their body, excepting their dominant arm and head. While the subject is lying supine, a target site for the subsequent TDC, SC, SBF, TEWL and Skin Temperature measurements will be marked on the dominant forearm 5 cm below the antecubital fossa.

Phase 1

Six preheat data sets will be acquired at two minute intervals from the target site in the following order: the subject's skin temperature, SC, tissue dielectric constants for 1.5 mm and 2.5 mm beneath the skin, and TEWL.

Phase 2

At this point the blood flow sensor and heating element will be attached to the skin at the target site. SBF will be continuously recorded until the end of Phase 4 via an analog to digital data acquisition system. The heating element will heat the skin to approximately 34° C and the blood flow will then be recorded once a minute for four minutes.

Phase 3

Next, the heating element will gradually increase heat applied to skin over approximately 1 minute, 30 seconds from 34° C to 40° C in single degree increments.

Phase 4

Once the 40° C steady state has been achieved, over the next 12 minutes once at the end of each minute, the blood flow will also be manually recorded from the perfusion monitor.

Phase 5

The heating element will now be deactivated and removed from the subject's forearm with the SBF sensor. Similarly as in Phase 1, skin temperature, SC, tissue dielectric constants for 1.5 mm and 2.5 mm beneath the skin, and TEWL will be measured, in that order at two-minute intervals for 12 minutes.

Final Data Collection and Clean-up

The subject's blood pressure will be measured in their dominant arm using a standard BP cuff. The electronic file for the continuous perfusion data will be saved. The subject will be thanked and receive their gift card, and probes will be sterilized with alcohol antiseptic wipes.

GENERAL PROCEDURE TIMELINE Total: 41 min, 30 sec.				
PHASE 1: 12 minutes	PHASE 2: 4 minutes	PHASE 3: 1 min, 30 sec	PHASE 4: 12 minutes	PHASE 5: 12 minutes
Collect probe measurements 6 times, at 2 minute intervals from target site.	Skin at 34˚C, SBF sensor and heat element applied.	Heating element increases target skin heat to 40˚C.	Maintain 40˚C target skin heat.	Collect probe measurements 8 times, at 2 minute intervals from target site.
Probe Measurements at Target Site: -Skin temp. -SC -TDC 1.5 mm -TDC 2.5 mm -TEWL	SBF, heat element applied to target site.			Probe Measurements at Target Site: -Skin temp. -SC -TDC 1.5 mm -TDC 2.5 mm -TEWL

D. Data Handling and Analysis:

The hypothesized dependence of tissue water on induced blood flow will be tested using regression analysis. Gender differences in measured parameters will be tested with independent T-tests with a p-value <0.05 accepted as significant.

References:

1. Pergola, P. E., D. L. J. Kellogg, et al. (1993). "Role of sympathetic nerves in the vascular effects of local temperature in human forearm skin. ." American Journal of Physiology 265(3): H785-792.
2. Minson, C. T., L. T. Berry, et al. (2001). "Nitric oxide and neurally mediated regulation of skin blood flow during local heating." Journal of Applied Physiology 91: 1619-1626.
3. Charkoudian, N., J. H. Eisenach, et al. (2002). "Effects of chronic sympathectomy on locally mediated cutaneous vasodilation in humans." Journal of Applied Physiology 92: 685-690.
4. Gooding, K. M., M. M. Hannemann, et al. (2006). "Maximum skin hyperaemia induced by local heating: Possible mechanisms." Journal of Vascular Research 43: 270-277.
5. Aimoto A, Matsumoto T. Noninvasive method for measuring the electrical properties of deep tissues using an open-ended coaxial probe. Med Eng Phys. 1996: 18(8): 641-6.
6. Alanen E, Lahtinen T, Nuutinen J. Measurement of dielectric properties of subcutaneous fat with open-ended coaxial sensors. Phys Med Biol. 1998: 43(3): 475-85.
7. Alanen E, Lahtinen T, Nuutinen J. Penetration of electromagnetic fields of an open-ended coaxial probe between 1 MHz and 1 GHz in dielectric skin measurements. Phys Med Biol. 1999: 44(7): N169-76.
8. Nuutinen J, Ikaheimo R, Lahtinen T. Validation of a new dielectric device to assess changes of tissue water in skin and subcutaneous fat. Physiol Meas. 2004: 25(2): 447-54.
9. Nuutinen J, Lahtinen T, Turunen M, Alanen E, Tenhunen M, Usenius T, et al. A dielectric method for measuring early and late reactions in irradiated human skin. Radiother Oncol. 1998: 47(3): 249-54.
10. Petaja L, Nuutinen J, Uusaro A, Lahtinen T, Ruokonen E. Dielectric constant of skin and subcutaneous fat to assess fluid changes after cardiac surgery. Physiol Meas. 2003: 24(2): 383-90.
11. Stuchly MA, Athey TW, Samaras GM, Taylor G. Measurement of radio frequency permittivity of biological tissues with an open-ended coaxial line: Part II - Experimental Results. IEEE Trans Microwave Theory and Techniques. 1982: 30(1): 87-92.
12. Stuchly MA, Athey TW, Stuchly SS, Samaras GM, Taylor G. Dielectric properties of animal tissues in vivo at frequencies 10 MHz--1 GHz. Bioelectromagnetics. 1981: 2(2): 93-103.

Part 4 – Sources of Data Information

Are you using questionnaires, tests, instruments, or forms?

Yes	No
X	

If "Yes", list them below and include a copy of each as appendices.

Physiological data recording form as attached to this proposal.

Do you plan to use any data from records or archives?

Yes	No
	X

If "Yes", please describe (such as data originally created for non research purposes or data created as a result of a previous study).

Do you plan to use any de-identified data?

Yes	No
X	

If "Yes", please describe the data and how it will be de-identified.

We will be asking the subject for the height, weight, age, gender and whether they drink caffeine regularly. The data will be de-identified because the subject's name will not be on the data collection sheet.

3. Additional Study Information

3.A. Clinical Testing

Food and Drug Administration
Investigational Drugs and Devices

Does the study involve the use of an investigational drug?

Yes	No
	X

If "Yes", has an Investigational New Drug application been submitted for the drug?

Yes	No

Does the study involve the use of an investigational device?

Yes	No
	X

If "Yes", has an Investigational Device Exemption (IDE) been, or will be, secured prior to the start of the study?

Yes	No

	Yes	No
Does the study use any device (either as a part of the experiment or to collect data) that has not received FDA approved for clinical/medical use or is being used in a manner not consistent with its cleared/marketing status?	X	

If "Yes", please describe the device and how its use differs from its approved status by the FDA.

TDC machine submitted for clearance to the FDA by company but not yet FDA clearance received.

Clinical Procedures

	Yes	No
Does the study involve the use of any procedure that is not used in routine clinical practice?	X	

If "Yes", please list the procedures.

TDC measurements, TEWL measurements, SC measurements, Skin Temperature measurements, Blood Flow measurement procedures.

3.B. Sensitive Information

	Yes	No
Are you asking questions about sensitive issues, such as illegal activity, sexual history, or anything else that, if made public, could jeopardize a person's reputation, employability, safety, or quality of life?		X

If "Yes", please describe the information.

	Yes	No
Does the study involve the collection of data from voice, video, digital, or image recordings made for research purposes?		X

If "Yes", please describe the procedures associated with these recordings.

3.C. Non-English Speaking Participants

	Yes	No
Will the study involve non-English speaking participants?		X
Will the study require translation of consent forms?		X

If you answered "Yes," please specify the language(s) that the consent forms will be translated in to:

If you are including non-English speaking participants, when you complete section III.H., please discuss how you will ensure that the participants understand the study, including the use of a qualified translator to

provide oral consent information.

3.D. Subject Compensation

Will your subjects receive any payments, incentives, or gifts?

Yes	No
X	

If "Yes," please indicate the types of compensation. Otherwise move on to section E.

Monetary Payment	Gift	Extra credit (Students) or Workplace Incentive (Employees)
X		

Other incentive

Please describe:

Participants will receive a $10 gift card for participating in and completing the study. Funds for these gift cards will be obtained from various unrestricted grants held by the principal investigator. If a subject starts the evaluation but does not complete they will not receive the gift. They will receive the gift card immediately after completion of their study.

Describe the payment(s)/gift(s)/incentive(s), and if it is a gift, estimate its monetary value. Indicate whether all participants are given the payment/gift/incentive, or if only some are eligible. (Note: the value of the payment/gift/incentive should not be so significant that it might compromise the subject's good judgment.)

Participants will receive a $10 gift card for participating in and completing the study. If a subject starts the evaluation but does not complete they will not receive the gift. They will receive the gift card immediately after completion of their study.

Describe when the subject will receive the payment/gift/incentive, and whether the amount differs depending upon whether different portions of the study are completed or is limited if the subject discontinues participation during the study.

They will receive the gift card immediately after completion of their study.

3.E. Inclusion / Exclusion Criteria for Subjects

Describe the inclusion and exclusion criteria for the proposed subjects. Please list the criteria in bullet or outline format rather than narrative. If the study limits participation based on gender, age or race, please justify the exclusion criteria. (Subject protection and appropriate study design may require specific inclusion or exclusion criteria, but the IRB does not permit subject selection that is not equitable or prevents a subpopulation from benefiting from the scientific discoveries of the study.)

Inclusion Criteria

1. Must be between 18 and 35 years of age

Exclusion Criteria

Subjects who have any of the following are excluded from participating:

1. Have implanted electrodes/wires/pacemaker
2. Have open wounds at sites of skin measurements
3. Has diabetes

3.F. Subject Recruitment

How will you recruit subjects (approach/invite/or ask people to be in your study)?

The physician co-investigators will advertise on University bulletin boards and in person for volunteer subjects using the possible incentive of gift cards or credit as participants in a research study.

Recruitment Advertisements, Fliers, and Letters

Are you using any letters, fliers, or advertisements?	Yes	No
	X	

If you answered yes, please list the type(s) below and attach a copy of the proposed materials as an appendix (do not copy and paste the flyer into this form).
(Note: Materials should list "Nova Southeastern University".)

3.G. Potential for Coercion in Subject Recruitment

Are any of the subjects a student or advisee of the PI or a Co-I?	Yes	No
	x	
Does the PI or a Co-I serve in any capacity (e.g., administrative, therapeutic) that might affect a subject's willingness to participate?	Yes	No
		X

If "Yes" to either of the above, then describe the relationship of the subjects and investigator.

If you answered yes, please read the NSU policy about use of students in research.
http://www.nova.edu/irb/manual/forms/research_students_subjects.pdf

Are any of the subjects employees of, or report to, the PI or a Co-I?	Yes	No
	X	
Are any of the subjects a patient of the PI or a Co-I?	Yes	No
		X
Are any of the subjects a patient within a PI or a Co-I's clinical practice?	Yes	No
		X
Are any of the subjects informed about the study by their doctor / clinician?	Yes	No
		X

If you answered "yes" to any of the questions in this section (3.G.), please describe how you will ensure that

the subjects will feel free to decline participation without fear of reprisal. If the subjects are patients, how will you prevent "therapeutic misconception" (the mistaken belief that when a care provider provides information about a study, it means that the provider thinks that study participation will benefit the patient).

The PI will have no knowledge of the students participating. No identification of the PI will be listed in the flyers, giving no other incentive for students to participate other than the gift card.

If you are providing any incentive to the student/employee subjects, discuss whether there is a mechanism for students / employees to receive the incentive by doing something other than participating in the research project (see http://www.nova.edu/irb/manual/forms/research_students_subjects.pdf).

Not applicable.

3.H. Informed Consent

Part 1 – Consent Process

Informed consent is a process that begins with advertising or telling potential subjects about your study, continues as the investigator or staff provides details to potential subjects via dialog, and is formalized by the signing of the consent.

Note: Minors must have consent of their parents or guardians before you can approach the minor about participating in the study.
Note: Allow as much time as possible and feasible for the subject to think about whether to enroll in the study. Generally, the greater the study risks, the longer the decision period.

Please overview the steps in the consent process in your research study. If there is more than one group of subjects, separately describe the process for each group.

Subjects will be female or male who are between the ages of 18 and 35. If a potential subject is interested, they will meet with a co-investigator, who will explain the study in detail and administer the consent form after collecting the subject's name, age, gender, height and weight.

Part 2 – Consent Process and Document Waiver/Alteration Information

In most cases, subjects need to participate in a meaningful consent process and receive a consent/assent form that documents agreement to participate in research. However, in a few cases the subject's confidentiality is protected by waiving/altering consent procedures or the requirement for signed consent forms. Please read the IRB's policy on informed consent for explanations, including what the IRB must demonstrate to permit waiver or alteration (http://www.nova.edu/irb/manual/forms/informed_consent.pdf). Please note, however, that while your study may qualify for waiver or alteration, that determination is at the discretion of the IRB.

One case where a signed informed consent form is NOT used is when a researcher is only reviewing existing/archival data that were collected for non-research purposes. If the data are obtained from the records by someone with authorization, and the data are de-identified, then it may be appropriate not to ask subjects (those whose data you are collecting) to provide consent, because the research involves no more than minimal risk, the waiver or alteration will not adversely affect the rights or welfare of subjects, the research could not practicably be carried out without the waiver or alteration, and, when appropriate, the subject will be provided pertinent information about participation. (NOTE: If your study has other

procedures that require interaction with subjects or prospective collection of data, it is unlikely that waiver or alteration of consent procedures or the signing of consent forms would be appropriate.) If this describes your study, then you may request a waiver of the requirement for informed consent and the documentation of signed consent.

If you think this applies in your study, please describe your rationale.

N/A

Another situation involving waiver or alteration of the requirement to obtain a signed consent form is when the research only entails conducting anonymous surveys that are not intrusive. If there is no way that the subjects' responses could be linked to them, then waiving the requirement for a signed consent form would minimize a risk to their confidentiality and privacy because the only record linking the subject and the research would be the consent form. If the principal risk would be potential harm resulting from a breach of confidentiality and the research presents no more than minimal risk to subjects and involves no procedures for which written consent is normally required outside of the research context, then the elements of informed consent are put into the survey itself. The person indicates his/her voluntary participation by completing the survey after being advised about the study and voluntary nature of his/her participation.

If you think this applies in your study, please describe your rationale.

N/A

There may be other cases where you would wish to ask for a waiver or alteration of informed consent or signed consent documentation.

If you are seeking a waiver or alteration, please describe your rationale.

N/A

Part 3 – Consent and Assent Document Information

Typically, you are asked to use the NSU format consent and assent forms. However, if this is cooperative research, or sponsored research that requires the use of a different template or model, you may use their format.

I will use NSU format consent/assent forms	X
I will be using another institution's format for consent/assent forms (NOTE: Please review the other institution's consent forms and the NSU requirements to be sure that all of the NSU requirements are present. You may also want to discuss the consent forms with your college/center representative)	
As noted above, I am requesting a waiver/alteration of consent and/or signed consent form requirements	

If you have different procedures for different groups of subjects, you will need a separate consent and/or assent form for each group. If the reading level of different groups of subjects differs, this may also require you to have different consent and/or assent forms (e.g. young children vs adolescents). If your subjects are children, you will also need parental consent.

What is the total number of consent/assent form types that you plan to use?

1

If using more than one consent form, create a list below that describes the different forms that you will be using (e.g. 1. Teacher consent form, 2. Parent consent form, 3. Assent form for children age 7-12, 4. Assent form for adolescents).

There will be one consent form.

Include copies of the consent / assent forms. When you attach the consent forms, put them in this order. Please note that the IRB prefers that the consent document be written using the simplest language possible, and strongly recommends the question and answer format (see Document Model #1 for Adult/General Consent Form [Readability Score: Grade 6]).

3.I. Protected Health Information Use

	Yes	No
Are you obtaining any data from the subject's medical record?		X
Are you asking the subject about his or her health information, and doing so in a clinic or entity that would normally be subject to HIPAA regulations on protected health information		X

If you answered "Yes" to either question, continue. Otherwise go on to section 3.J.

Please review the NSU HIPAA research policies available at (http://www.nova.edu/irb/manual/policies.html for more information.

Please note that effective 12/10/2009 the NSU IRB no longer reviews separate HIPAA authorizations for research. It is the principal investigator's responsibility to use the correct HIPAA authorization as outlined in the aforementioned policy. In instances where the HIPAA authorization must be a part of the informed consent form for research, the NSU IRB will review the compound consent.

Specify the exact data to be gathered (e.g., weight, blood pressure, IQ score, diagnosis, depression rating, number of treatments, etc.).

Which procedure are you proposing to use? (Check)	
I will obtain the subject's authorization to obtain the protected health information via the NSU Authorization for Use and Disclosure of Protected Health Information in Research (research activities will be occurring at an NSU clinic).	
I will obtain the subject's authorization to obtain the protected health information via the authorization for use and disclosure of protected health information in research provided by the non-NSU covered entity.	
The protected health information data are a fully de-identified data set (data obtained without recording any patient information, with the data accessed by an employee of the institution).	
The data are part of a limited data set agreement as defined by the Office of Human Research Protections. (Attach a copy of the agreement.)	

If part of a limited data set agreement, what is the justification that confidentiality is protected?

I have a waiver provided by a duly constituted privacy board. (Attach a copy of the waiver.) ☐

HIPAA Research Authorization

If the research is to be conducted at an NSU clinic, have you created a HIPAA authorization form as outlined in the HIPAA Research Policy No. 1 (http://www.nova.edu/irb/manual/policies.html) and in keeping with the Instructions for Preparing the Authorization For Use and Disclosure of Protected Health Information in Research Form and the model form provided (http://www.nova.edu/irb/manual/forms.html)?

Yes ☐ No ☐

Please note, do NOT submit a copy of the HIPAA authorization form if you are following the model noted in the aforementioned policy.

If the research is to be conducted at a non-NSU covered entity, have you reviewed the HIPAA Research Policy No. 6: Guidance on Research at Outside Entities (http://www.nova.edu/irb/manual/policies.html)?

Yes ☐ No ☐

Researchers are advised to discuss the proposed research with the applicable HIPAA privacy officer at the non-NSU covered entity.

Does the researcher sponsor or cooperating agency require the incorporation of the HIPAA authorization within the consent document (Compound Consent)?

Yes ☐ No ☐

If yes, please briefly indicate who requires that this be in the informed consent document.

Please note, consent forms that include the HIPAA authorization may need approval from the university Office of Corporate Compliance.

3.J. Student/Academic Information Use

Are you obtaining any data from the subject's academic records?

Yes ☐ No ☒

If you answered "Yes", continue. Otherwise go on to section K.

Specify the exact data to be gathered (e.g., GPA, standardized test score, IQ score, medical/psychological information stored in academic files, attendance records, disciplinary records, etc.).

Specify how you will obtain the data.

Which procedure are you proposing to use? (Check all that apply)

I will obtain the subject's consent to obtain the academic information.

The academic information will be a part of a fully de-identified data set (data obtained without recording any subject information, and provided to you in keeping with the institution's policies and the Federal Educational Rights and Privacy Act [FERPA]).

3.K. Risks, Discomforts, & Inconveniences

In this section, discuss all potential risks (physical, economic/financial, legal, psychological, social, etc.), discomforts, or inconveniences to the subjects.

- All studies using identifiable subject information must address the issue of possible loss of subject confidentiality
- Some possible risks include physical, psychological or emotional harm, breach of confidentiality, and invasion of privacy.
- Discomfort includes anticipated risk for mild physical or emotional pain.
- Study inconveniences include loss of time or pay.

Each risk, discomfort and inconvenience should be addressed individually in the following format (use the tables provided and copy if the study presents more than 3).

- List each risk individually
- Discuss likelihood: How likely is it that this risk/discomfort or inconvenience will occur? This is usually classified as minimal, moderate, or high.
- Discuss magnitude/duration: How dire is the risk/inconvenience/discomfort, and if it occurs, how long do you expect that the subject will be affected?
- Discuss risk minimization: Describe the procedures undertaken to minimize the risk that this specific risk/discomfort/inconvenience will occur.

Risk/Discomfort	Some discomfort during cuff inflation during BP measurements
Likelihood	Likely
Magnitude/Duration	Few seconds
Risk Minimization	Release the pressure on the cuff

Risk/Discomfort	Possible minor discomfort and redness from skin heating procedure.
Likelihood	Possible but minor
Magnitude/Duration	12 minutes
Risk Minimization	If discomfort not tolerable by subject, will abandon study on this subject.

Risk/Discomfort	
Likelihood	
Magnitude/Duration	
Risk Minimization	

One way in which confidentiality is partially protected is to destroy study documents containing identifiable information when they are no longer needed. The IRB requires that study materials be kept for a minimum of three years from the end of the study to permit study auditing; you may elect to keep them for a longer period of time and study sponsors may have their own data retention requirements. Please indicate when and how you plan to destroy data that contains identifiable subject information, such as consent forms, lists that link subject identity to data coding, or raw data containing subject names.

With respect to data security, any data (hard copy or electronic) collected and used for analysis will be identified only with a random number. This random number will be placed on a copy of the consent form and stored in a locked filing cabinet in Room 1313. All records will be stored for five years, before being destroyed.

3.L. Benefits to Subjects

In this section, discuss all direct benefits of the study to participants. This does not include "helping research" or other generalities, nor does it include compensation for participation. Some examples of benefits include receiving free treatment, receiving a list of reputable local services, or obtaining tutoring. The value of any such benefits should be listed as well. If there are no direct benefits to the participants, this should be indicated.

Are there any direct benefits to the research participants?

There are no direct benefits to study participants [X]

This study provides benefit to, or is likely to benefit, the participants [ ]

List/describe each benefit

N/A

3.M. Data Analysis Plan

Please describe preliminarily proposed data analysis procedures.

The hypothesized dependence of tissue water on induced blood flow will be tested using regression analysis. Gender differences in measured parameters will be tested with independent T-tests with a p-value <0.05 accepted as significant.

3.N. Scientific Benefit

Briefly discuss how generalization of the information obtained from this study will be scientifically useful, or useful to your research site.

Results of this study could help to provide a foundation for novel skin heating therapies to modulate tissue water as part of the treatment of various pathologies. In addition, the results found through conducting this study are of fundamental importance to the science of physiology and will serve to benefit the scientific community.

3.O. Risk/Benefit Ratio

To be approved, a study needs to have greater benefits than risks. Why do you believe this study has a positive benefits-to-risks ratio?

The risk approaches zero while the scientific data collected on skin temperature, SC, TDC, TEWL, and blood perfusion will be a novel addition to the scientific literature on the subject.

3.P. Safety Monitoring Plans

All researchers are required to report adverse events and unanticipated problems in keeping with the NSU IRB policy (http://www.nova.edu/irb/manual/forms/adverse_events.pdf).

Studies that entail significant risk to subjects, such as randomized controlled drug trials, may warrant safety monitoring by an outside safety board. Does your study utilize a Data Safety Monitoring plan?

Yes	No
	X

If "Yes," please describe the safety monitoring plans. Please specify if the study will be monitored by the investigators, sponsors (if applicable), or a Data Safety Monitoring Board (DSMB). Sponsored studies may reference an attached Investigator Brochure.

3.Q. Other Information

If there is other information about this study that is required in order for those reviewing the study to fully understand the study, its risks and benefits, please describe below.

N/A

3.R. Principal Investigator Assurance and Obligations

I certify that all information provided in this submission (including any supporting documents) is a complete and accurate description of the proposed study. I agree to the following:

This study will be conducted in the manner described in this submission and will not be implemented (including subject recruitment or consenting) until all applicable IRBs have granted permission to conduct the research. No changes to this study will be implemented until an amendment form has been submitted and approved by the IRB.

PI Initials	HNM

If the IRB approves this study via expedited or full procedure, I will submit for continuing review as stipulated in the approval letter. If the study or data analysis will exceed the approval period, I will submit a Submission Form for Continuing Review of IRB Approved Studies in a timely manner (well in advance of the renewal date).
I understand that study activities may not continue past an approval period.

PI Initials	HNM

I will provide a copy of the signed consent form to the subject or patient, if applicable.

PI Initials	HNM

I will retain all signed informed consent documents and study-related records for a minimum of three (3) years (or longer as stipulated by funding agencies) from the date the study is concluded.

PI Initials	HNM

I will report in writing any serious adverse events to the IRB within 24 hours and all other adverse events and unanticipated problems within 5 working days.

PI Initials	HNM

I will provide participants with any significant new information obtained during the course of the study and submit reports of new information to the IRB as a Study Amendment.

PI Initials	HNM

If my study has been approved at the Expedited or Full Review levels, I will report to the IRB when this study has closed (no further data collection or analysis). This report will be provided no later than 30 days after the end of the study via the IRB Closing Report Form.

PI Initials	HNM

Principal Investigator's Signature: _____Date: _____

3.S. Co-Investigator Assurance and Obligations (for Student PIs)

If this study is for the completion of a degree requirement, the thesis adviser or dissertation chair must sign the attestation below.

- All departmental approvals by the student's committee (if applicable) and chair or thesis adviser have been completed.
- I accept that the University and IRB consider the faculty advisor's responsibility to be equal to that of the student in regard to
    - The quality of the research design AND the accuracy of the protocol
    - The appropriateness of the recruitment methods, the design of the process for informing the subjects about the nature of the study, and the process of obtaining informed consent
    - The readability, accuracy, and format of the informed consent/assent document(s) and the explanation of all informed consent procedures.

My signature below attests that I have read this submission in its entirety and believe that it is accurate, complete, appropriate, and adheres to the principles of the Belmont report and that all departmental approvals by the student's committee have been completed.

NA

Appendix 1

Advertisement as it will appear:

Appendix 2. Data Entry

FOREARM DATA: Heat-TDC-SC-TEWL on dominant forearm 6 cm distal to AC SC to be measured at device own weight. TDC device =								
id	date	Time	Age	gender (0,1)	dom (1,2)	ht(in)	wt(lbs)	bmi

Pre-Heat Measurements							
#	Tskin	SC	TDC_1.5	TEWL	TDC_2.5	Troom	RH
1							
2							
3							
4							
5							
6							
AVG							
SD							
AVG + 2SD							

Heat AT TARGET DEVICE TEMP (44) for 12 minutes to achieve 40°C							
Post-Heat	Time to reach TARGET TEMP SETTING in seconds						
min interval	Tskin	SC	TDC_1.5	TEWL	TDC_2.5	Troom	RH
0							
2							
4							
6							
8							
10							
12							
14							
16							
18							
20							

The following is related to the skin blood flow measurements				
LDF probe serial number			LDF Unit	Vasamedic Unit #2
Time Constant Used			Sensitivity	

The following are flow values read from meter in ml/min/100g at each min pre-heat and after target reached					
PRE-HEAT		DURING HEATING AFTER TARGET REACHED			
min	FLOW	min	FLOW	min	FLOW
1		1		7	
2		2		8	
3		3		9	
4		4		10	
		5		11	
		6		12	
AVG		AVG			
SD		SD			

Form