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:

Investigation of glycosylation effects on skin-to-fat tissue water content in persons with diabetes mellitus assessed by skin tissue dielectric constant (TDC)

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

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

It has been estimated by the International Diabetes Foundation that there are about 285 million people around the world living with diabetes and that approximately one third of this population undergo some form of skin manifestations. While patients with type I diabetes are more likely to suffer from autoimmune related lesions, patients with type II diabetes are more prone to cutaneous infections. Ultrasound research shows that diabetic patients have thinner skin and less subcutaneous fat compared to age-matched control subjects, which supports the idea that such biophysical changes may alter the

skin-to-fat tissue water content which can then alter skin functions. Literature further supports the idea that the excess supply of glucose leads to non-enzymatic chemical reactions between the carbonyl group of glucose and amino acids of proteins and this glycation of structural and regulatory proteins plays a key role in the pathogenesis of diabetic skin complications such as diabetic ulcer or diabetic foot syndrome. However it is not clear whether the changes in tissue water content affect normal skin maintenance. Since the glycosylation of structural proteins strongly adheres glucose molecules to the protein, a plausible hypothesis is that diabetic persons with higher HbA1c values will have less tissue water content compared with persons with lower HbA1c values. Thus, our main goal is to determine the correlation between skin-to-fat tissue water as measured by tissue dielectric constant (TDC) and HbA1c amongst patients with diabetes. This study may be viewed as a pilot investigation of the possible correlation between these two important parameters.

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*	
		09/06/2011	

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	Naushira Pandya	Bansari Sarkar	Irina Volosko
Mailing Address	3200 University Drive Fort Lauderdale, FL 33328	3625 College Avenue Rolling Hills Box 1825 Davie, FL 33328	5950 Toscana Drive, apt 522, Davie, FL 33314
Contact Phone Number	954-262-4100	201-238-8591	415-570-1275
Email Address	pandya@nova.edu	bs1200@nova.edu	iv86@nova.edu
Degree/Academic Information:	MD	1st year osteopathic medical student	1st year osteopathic medical student
CITI Completion Date*		01/07/2014	01/18/2014

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

Bansari - B.A. in Cell Biology and Neuroscience, 4 years of research experience.
Dr. Pandya - M.D.
Irina - M.S. in Biochemistry, 4 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.

HPD Clinic

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 approved)	Not yet submitted	NSU IRB approval required prior to 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*						**80**		

Please briefly describe your potential subjects:

The main source of subjects will be patients of Dr. Pandya diagnosed with either type I or type II diabetes. We are planning to have equal numbers of males and females.

*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	
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.

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".

The main goal of the study is to test the hypothesis that there is a significant correlation between glycosylation as measured by glycated hemoglobin (HbA1c) values and skin-to-fat tissue water content as measured by TDC of persons with diabetes. A secondary goal of this study is to explore the possible role of gender in skin TDC values in persons with diabetes.

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.

Previous research has established that the diabetic condition often entails changes in blood flow and blood vessels in the skin (1-3) however there is not much explanation offered as to the reasons for the biophysical changes in the skin. It has been thought that skin homeostasis could be disrupted through either diabetic-induced changes in skin metabolism or through associated complications such as vasculopathy and neuropathy. Recent research using ultrasound has shown that persons with diabetes have thinner skin (epidermis plus dermis) and less subcutaneous fat than age-matched people without diabetes (4). These results suggest that structural changes within the skin may affect tissue water content, either directly or indirectly. Literature supports the view that hyperglycemia-induced non-enzymatic glycation of structural and regulatory proteins play a major role in the pathogenesis of diabetic complications (5). This is known as the Maillard reaction in which the excess supply of glucose in the blood plasma leads to the non-enzymatic chemical reaction between the carbonyl group of glucose and the amino acid of proteins (5). However the influence of excess glucose in the diabetic condition on the hydration of the stratum corneum is still heavily controversial. While Sakai et al. (6) discovered reduced stratum corneum hydration levels, a lower level of skin surface lipids, and decreased sebum secretions in diabetic mice, Seirafi et al. (7) did not detect a difference in stratum corneum hydration between diabetic and healthy patients. Thinning of the dermis decreases relative water content whereas subcutaneous fat loss increases skin-to-fat water content since the water content of fat is low. Additionally excess glycation of proteins tends to create and accumulate advanced glycation end products (AGEs), which contribute to the pathogenesis of various diabetic disorders (8-10). Thus, our goal is to determine the correlation between skin-to-fat tissue water as measured by tissue dielectric constant (TDC) and HbA1c amongst patients with diabetes. This study may be viewed as a pilot investigation of the possible correlation between these two important parameters. The non-invasive TDC method will be the basis for measuring skin tissue water. This method has already been successfully implemented to evaluate the levels of local tissue water in the arms and legs of patients with breast cancer, patients with lymphedema, as well as healthy patients (11-16). As an additional component of this study, we will also examine the potential impact gender impacts on TDC values in persons with diabetes.

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. Protocol:

During a scheduled clinical visit at the HPD Geriatrics Clinic, Dr. Pandya, the physician co-investigator will inform the subjects as to the existence of the research study. If a subject is interested she/he will meet with a co-investigator, who will explain the study in details and administer the consent form. The procedure for all enrolled subjects will be as follows, with all measurements done in the HPD Geriatrics Clinic of Nova Southeastern University.

Each subject will be asked to remove her/his shoes and socks and then be asked to step onto a bioimpedance scale (Ironman InnerScan Body Composition Monitor, Tanita BC-558, Tokyo, Japan) and grip two attached handles for a period of about 20 seconds. This will allow obtaining the subject's weight, and percentages of body water and fat. This measurement takes about one minute in total. Next the subject will be asked to lie supine on an examination table. While lying, the target sites for the subsequent TDC measurements will be marked on the dominant side of the subject's body on the forearm, lower leg and foot. These TDC measurements are to be performed in triplicate at the following locations; on the forearm—6 cm below the antecubital fossa, on the leg—10 cm proximal to the lateral malleolus, and on the dorsum of the foot at a site close to the junction of the 1st and 2nd toes. Each TDC measurement will be made to effective depths of 0.5, 1.5, 2.5, and 5.0 mm as further described in section B. Approximate time required for the TDC measurements is nine minutes. Following the TDC measurements, the subject's blood pressure will be made in triplicate with the subject still supine. Blood pressure will be measured simultaneously in both arms using a dual pressure measuring device (Microlife Watch BP office Twin 200). This measurement takes about two minutes. The total measurement time is estimated to be about 15 minutes. Each subject will be measured during only one visit.

B. Method for Measurement of Local Tissue Water via Tissue Dielectric Constant (TDC)

The process of assessing local tissue water is based on the principle that TDC is directly related to the amount of free and bound water contained in a measuring volume (17-25). The TDC is a dimensionless quantity that is the ratio of the absolute tissue dielectric constant to that of free space. The TDC value of a specific target area is determined using a coaxial probe that gently contacts the skin for approximately 10 seconds; the probe which is connected to a control and display device measures the TDC value at a frequency of 300 MHz. Pure water has a TDC value of about 78.5. For the purpose of this study, the TDC measurements will be taken at effective depths of 0.5, 1.5, 2.5, and 5.0 mm. Measurements will be made at three anatomical sites; the forearm 6 cm below the antecubital fossa, 10 cm proximal to the lateral malleolus, and between the first and second toes on the dorsum of the foot. All three sites will be measured only on the dominant side of the body. Each measurement with each probe will be made in triplicate starting with the 5.0 mm probe and progressing towards the 0.5 mm probe. The time required for completing a triplicate tissue water measurement is about 45 seconds. This means that the total time requirement to complete TDC measurements for all four probes, taking into account the time needed to change probes, is approximately nine minutes.

C. Data Handling and Analysis

The main goal of this study is to test the hypothesis that in persons with diabetes mellitus TDC values, used as index of skin-to-fat tissue water, significantly correlates with the level of HbA1c. Consequently the main analysis procedures will be based on the following null and alternate hypothesis. The null hypothesis (H0) is that there is no correlation among the two variables and the alternate hypothesis (Ha) is that there is a correlation. Based on the judgment that a fundamentally meaningful and potentially clinically useful relationship would need a correlation coefficient (r) of at least 0.45 in magnitude, this effect size (r=0.45) has been chosen for the present study. To test for this effect size at a α level of 0.01 and β level of 0.05 requires a study population (N) equal to 79 which has been rounded up to a target group size of N=80. The chosen target α value is consistent with a probability of making a type 1 error equal to 5% (rejecting H0 when H0 is true, i.e. false positive finding). The chosen target β value is consistent with a probability of making a type 2 error of 5% (failing to reject H0 when H0 is false, i.e. false negative finding). This β-level corresponds to a power of 95% (i.e. a 95% chance of finding a correlation equal to the effect size). The composite of the Individual TDC values and corresponding HbA1c values will constitute the paired values for the correlation analysis. Although TDC values will be measured at multiple depths (0.5, 1.5, 2.5 and 5.0 mm), previous work has shown that these values are highly correlated ($p<0.001$). Thus, in order not to reduce statistical power of the primary correlation analysis, it is a priori planned to use only the 2.5 mm depth TDC in the correlation analysis. The depth data will be used separately to characterize the depth dependence of TDC values in this diabetic population and to compare values between genders. TDC data from the three anatomical sites (forearm, lower leg and foot) are viewed as independent assessments since prior work has shown significant differences in TDC values among sites in persons without diabetes. Thus separate correlation analysis of HbA1c vs. TDC @ 2.5 mm and will be done for each site. Depth dependence of TDC values will be determined separately at each anatomical site. This is achieved by characterizing the TDC vs depth characteristic for each site using regression analysis. The comparisons among the three sites are done by comparing the regression coefficients that essentially represent the TDC-depth slope using analysis of variance (general linear model) for repeated measures. To investigate possible gender differences, these slopes and absolute TDC values will be compared between genders with each site analyzed separately. The possible impact of clinical parameters, including blood parameters, blood pressure and ABI on TDC-HbA1c relationships will be examined using stepwise regression methods.

REFERENCES

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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).

Age
Height
Weight
Blood pressure
Duration of diabetes
Basic metabolic panel
Most recent HbA1c values (< 6 months)
Most recent blood glucose values
Current diabetes medication usage
History of lower extremity arterial disease
Current medication list
Presence of renal arterial disease

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.

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

	Yes	No
Does the study involve the use of an investigational device?		X

	Yes	No
If "Yes", has an Investigational Device Exemption (IDE) been, or will be, secured prior to the start of the study?		

	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 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 at least 18 years of age
2. Must have been diagnosed with diabetes mellitus (either type I or type II)

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 TDC measurements

3.F. Subject Recruitment

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

In the case of persons with diabetes who are being seen clinically by Dr. Pandya, she will determine the potential suitability of their participation and if so discuss the research study with the person and determine if they are interested in participating. If there is interest then Dr. Pandya will refer the patient to a co-investigator who will be present in the clinic. The co-investigator will describe the study in detail and if the person wishes to participate the informed consent form will be administered.

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.

Some subjects might be patients being seen by one of the Co-investigators (Dr. Pandya)

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?	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).

A potential participant will be informed previously by Dr. Pandya that the measurements that will be made as a part of this research study will have no therapeutic value and that the potential diagnostic usefulness of the measurements at this time is unknown and to be determined from the study findings and results.

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.

A co-investigator will describe the study to potential participants, answer any questions they may have and oversee the administration of the consent form. All potential participants will be given the opportunity to meet with the principal investigator (Dr. HN Mayrovitz) prior to (or after) consenting if they should so desire.

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.).

Age
Height
Weight
Blood pressure
Duration of diabetes
Basic metabolic panel
Most recent HbA1c values (< 6 months)
Most recent blood glucose values
Current diabetes medication usage
History of lower extremity arterial disease
Current medication list
Presence of renal arterial disease

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).	X
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
X	

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
☐	X

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	Loss of confidentiality
Likelihood	Minimal
Magnitude/Duration	Five years
Risk Minimization	All information obtained in this study is strictly confidential unless the law requires disclosure. To avoid the risk of possible loss of confidentiality, all records and signed consents will be kept and protected for five years. Only the principle and co-investigators will have access to this information. Any data collection form with your data will only have a randomly assigned number. This code number will also be inscribed on your consent form. A list with the participant names and code numbers along with any data collection forms and the consent form will be kept in separate locked cabinets in room 1313 of the Terry Building. Dr. Mayrovitz will hold the key to these cabinets. Data will be safely locked away for 60 months from conclusion of the study, after which it will be shredded. If the results of the study are released or published for scientific or any other purpose you will not be identified by name. If necessary, the IRB and regulatory agencies may review research records.

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.

No forms other than the consent forms will contain the same of the study subjects. These will subsequently be destroyed after 5 years.

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 main goal of this study is to test the hypothesis that in persons with diabetes mellitus TDC values, used as index of skin-to-fat tissue water, significantly correlates with the level of HbA1c. Consequently the main analysis procedures will be based on the following null and alternate hypothesis. The null hypothesis (H0) is that there is no correlation among the two variables and the alternate hypothesis (Ha) is that there is a correlation. Based on the judgment that a fundamentally meaningful and potentially clinically useful relationship would need a correlation coefficient (r) of at least 0.45 in magnitude, this effect size (r=0.45) has been chosen for the present study. To test for this effect size at a α level of 0.01 and β level of 0.05 requires a study population (N) equal to 79 which has been rounded up to a target group size of N=80.

The chosen target α value is consistent with a probability of making a type 1 error equal to 5% (rejecting H0 when H0 is true, i.e. false positive finding). The chosen target β value is consistent with a probability of making a type 2 error of 5% (failing to reject H0 when H0 is false, i.e. false negative finding). This β-level corresponds to a power of 95% (i.e. a 95% chance of finding a correlation equal to the effect size).

The composite of the Individual TDC values and corresponding HbA1c values will constitute the paired values for the correlation analysis. Although TDC values will be measured at multiple depths (0.5, 1.5, 2.5 and 5.0 mm), previous work has shown that these values are highly correlated ($p<0.001$). Thus, in order not to reduce statistical power of the primary correlation analysis, it is a priori planned to use only the 2.5 mm depth TDC in the correlation analysis. The depth data will be used separately to characterize the depth dependence of TDC values in this diabetic population and to compare values between genders. TDC data from the three anatomical sites (forearm, lower leg and foot) are viewed as independent assessments since prior work has shown significant differences in TDC values among sites in persons without diabetes. Thus separate correlation analysis of HbA1c vs. TDC @ 2.5 mm and will be done for each site.

Depth dependence of TDC values will be determined separately at each anatomical site. This is achieved by characterizing the TDC vs depth characteristic for each site using regression analysis. The comparisons among the three sites are done by comparing the regression coefficients that essentially represent the

TDC-depth slope using analysis of variance (general linear model) for repeated measures. To investigate possible gender differences, these slopes and absolute TDC values will be compared between genders with each site analyzed separately. The possible impact of clinical parameters, including blood parameters, blood pressure and ABI on TDC-HbA1c relationships will be examined using stepwise regression methods.

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.

It will provide potential data relating TDC values with HbA1c values which has been previously undocumented which is useful to further scientific research into skin manifestations of the diabetic condition.

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 TDC and HbA1c values will be a significant and valuable addition to the scientific literature on diabetes.

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.

Chair/Adviser's Signature: _____ Date: _____

Appendix

Physiological Data Recording Form

			0=F 1=M				1=R 2=L			
id	Date	Time Lay	Sex	Age	Ht (in)	Wt (lbs)	Dom Arm	Trm	RH	BMI

Body Fat	LA	RA	RL	LL	TRUNK	TOTAL	Total H_2O %
Muscle Mass	**LA**	**RA**	**RL**	**LL**	**TRUNK**	**TOTAL**	

TDC start time	1/11/1900	Tdc values			Avg	Avg	Avg
Probe	M#	Forearm	Leg	Foot	Forearm	Leg	Foot
5.0 mm	1						
	2						
	3						
2.5 mm	1						
	2						
	3						
1.5 mm	1						
	2						
	3						
0.5 mm	1						
	2						
	3						

Blood Pressure Cuff Placement

CUFF A (the one with Right dot) is on the		arm
CUFF B (the one with Left dot) is on the		arm

Time BP start	PRESSURES (mmHg)					Pressure Differences	
	LEFT ARM		RIGHT ARM			SYS	DIA
PAIR #	SYS	DIA	SYS	DIA	HR	R - L	R-L
1							
2							
3							
AVG							
SD							
CV(%)							

TDC done by		BP done by		Time end