Form A

IRB #	STU STU-2018-0386

PROTOCOL FORM / RESEARCH DESCRIPTION

If an item does not apply to your research project, indicate that the question is "**not applicable**" – do not leave sections blank

Click once on the highlighted entry in each box to provide your response. Click the item number/letter or word, if hyperlinked, for detailed instructions for that question. If your response requires inserting a table, picture, etc, you may need to first delete the box that surrounds the answer and then insert your table or other special document.

1. Purpose and objectives. *List the purpose and objectives:*

One of the unmet needs in wound healing are tools to assess peripheral vascular disease, wound healing, and amputation level selection. There are several commercial available devices that are non-contact and acquire and record data in a few seconds using near infrared light therapy. While these devices are FDA approved there is little evidence to understand how to interpret the data.

Patient group: We will prospectively collect data using one instrument (camera) (Snapshot NIH, Kent Imaging, Calgary, Alberta, Canada). We will collect non-contact imaging data before surgeries, during surgeries (if feasible), and during follow-up clinic visits. We will collect vascular data, demographic medical history, wound characteristics and measurements, frequency of debridement, off-loading, and clinic visits from existing medical records. We will collect lab data such as cultures glycosylated hemoglobin, hemoglobin and hematocrit, ESR, CRP and eGFR obtained per standard of care.
Imaging with this device is research-only.

Normal group: We will also collect normative data from healthy individuals to include baseline data, screening, and images. Up to 500 people will be enrolled and can include normal healthy volunteers, staff and students/trainees. Data will be collected one time with no follow up. The PI will not be a participant.

Specific Aims:
Aim 1. To evaluate the effectiveness of the Kent instrument to measure perfusion to predict wound healing, flap survival and amputation level healing.

2. Background.

- Describe past experimental and/or clinical findings leading to the formulation of your study.
- For research involving investigational drugs, describe the previously conducted animal and human studies.
- For research that involves FDA approved drugs or devices, describe the FDA approved uses of this drug/device in relation to your protocol.
- Attach a copy of the approved labeling as a product package insert or from the Physician's Desk Reference.

You may reference sponsor's full protocol or grant application (section number and/or title) or if none, ensure background includes references.

Please respond to all components of this item, or clearly indicate which components are not applicable.

a. Background

There is a worldwide epidemic of diabetes. According to data from the World Health Organization, the world prevalence of diabetes among adults was 6.4% in 2009, affecting 285 million adults worldwide. The prevalence of diabetes is expected to increase to 7.7% by 2030 (439 million adults) (1). In the United States, the prevalence of diabetes increased by 26% from 2007 to 2012, and the associated cost of managing this disease increased from $174 to $245 billion (41% increases) in the same time period (2, 3). Recent studies show that the lifetime risk of an American born between 2000 and 2011 have a probability of developing diabetes is 40%, emphasizing the need for further study and optimization of their care (4). Diabetic foot infections are a common, costly, and life altering complication.

As part of the worldwide epidemic of diabetes mellitus, the prevalence of lower extremity complications is rising. Patients with diabetes are now confronted with a 25% lifetime risk of developing a foot ulcer (5). Among persons with diabetes, foot infections are one of the most common reasons for hospitalization and lower extremity amputations and occur approximately 60% during the life of the ulceration (6). Patients with diabetic foot osteomyelitis have a 4-22-fold increased risk of amputation, more proximal amputation, and longer hospital stays (7-9).

b. Current practice

Preliminary Studies:

Our group has completed several studies to support this review. In addition, we have published data from a large cohort study (N=1,666) that reported patient characteristics, risk factors and clinical outcomes of diabetic patients with foot infections, as well as studies that describe the epidemiology and the treatment of diabetic foot osteomyelitis (7, 10-13).

References:

1. World Health Organization Global report on diabetes: World Health Organization; 2016.

2. American Diabetes Assocation Economic Costs of Diabetes in the U.S. in 2012. Diabetes care. 2013;36(4):1033-46. PMCID: 23468086.

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4. Gregg EW, Zhuo X, Cheng YJ, Albright AL, Narayan KMV, Thompson TJ. Trends in lifetime risk and years of life lost due to diabetes in the USA, 1985–2011: a modelling study. The Lancet Diabetes & Endocrinology. 2014;2(11):867-74. doi: 10.1016/s2213-8587(14)70161-5.

5. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293(2):217-28. doi: 10.1001/jama.293.2.217. PubMed PMID: 15644549.

6. Prompers L, Huijberts M, Apelqvist J, Jude E, Piaggesi A, Bakker K, Edmonds M, Holstein P, Jirkovska A, Mauricio D, Ragnarson Tennvall G, Reike H, Spraul M, Uccioli L, Urbancic V, Van Acker K, van Baal J, van Merode F, Schaper N. High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. Diabetologia. 2007;50(1):18-25. doi: 10.1007/s00125-006-0491-1. PubMed PMID: 17093942.

7. Lavery LA, Peters EJ, Armstrong DG, Wendel CS, Murdoch DP, Lipsky BA. Risk factors for developing osteomyelitis in patients with diabetic foot wounds. Diabetes Res Clin Pract. 2009;83(3):347-52. doi: 10.1016/j.diabres.2008.11.030. PubMed PMID: 19117631.

8. Wukich DK, Hobizal KB, Sambenedetto TL, Kirby K, Rosario BL. Outcomes of Osteomyelitis in Patients Hospitalized With Diabetic Foot Infections. Foot & ankle international / American Orthopaedic Foot and Ankle Society [and] Swiss Foot and Ankle Society. 2016;37(12):1285-91. doi: 10.1177/1071100716664364. PubMed PMID: 27553085.

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10. Lavery LA, Armstrong DG, Peters EJG, Murdoch DP, Lipsky BA. The “Probe to Bone” Test for Diagnosing Osteomyelitis of the Foot in Persons with Diabetes: Reliable, or Relic? Diabetes. 2005;54 (Suppl1):65(OR).

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12. Lavery LA, Lavery DC, Hunt NA, La Fontaine J, Ndip A, Boulton AJ. Amputations and foot-related hospitalisations disproportionately affect dialysis patients. Int Wound J. 2015;12(5):523-6. doi: 10.1111/iwj.12146. PubMed PMID: 24103293.

13. Lipsky BA, Aragon-Sanchez J, Diggle M, Embil J, Kono S, Lavery L, Senneville E, Urbancic-Rovan V, Van Asten S, International Working Group on the Diabetic F, Peters EJ. IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. Diabetes Metab Res Rev. 2016;32 Suppl 1:45-74. doi: 10.1002/dmrr.2699. PubMed PMID: 26386266.

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3. Study Design.
Describe the study design (e.g., single/double blind, parallel, crossover, etc.) Consider inserting a scheme to visually present the study design.

This is a prospective, observational study.

Patient group: All medical and surgical care provided to the patient will be standard of care.

Once a patient is identified as requiring vascular intervention or a lower extremity ulceration (includes lower extremity wound of any cause, a surgical incision, a flap or graft) and consents to participation, their lower extremity will be imaged per protocol in part 4 below. They will be imaged preop, intraop (if feasible) and on post-op day 1 + or – 7 days if they require surgery and for each surgery related to the ulceration. They will also be imaged once a month in follow up for up to 6 months or healing of the wound, determined by study physician.

Normal group: The normal group will have one-time imaging and data collection.

4. Research Plan / Description of the Research Methods:

4.a. Provide a **comprehensive narrative** describing the **research methods**.

1) Provide the **order in which tests/procedures will be performed**,
2) Provide the **setting** for these events and a description of the **methods used to protect privacy** during the study.
3) Provide the **plan for data analysis** (include as applicable the **sample size calculation)**

Please respond to all components of this item, or clearly indicate which components are not applicable.

1) All *treatment* received both medically and surgically will be rendered as standard of care for the patient group. This is an observational prospective study. Imaging with the two devices is research-only and is not standard of care.
Data will be collected with 1 vascular imaging device (Snapshot NIH, Kent Imaging, Calgary, Alberta, Canada). The wound will be imaged with the device at index research encounter (this will count as the initial pre-operative imaging if the patient requires surgery), before surgery for interval or additional surgeries, during surgery (if feasible), and during clinic follow-up (one set of imaging approximately every 3-5 weeks) visits for a maximum follow up time of 6 months or until the wound is documented as healed, whichever occurs first. We will collect images from the lateral, dorsal, and plantar aspects of the foot. Subject data will be obtained from the patient by oral history and physical exam and the medical records of patients of the investigators: vascular data, demographic medical history, wound characteristics and measurements, frequency of debridement and off-loading. Collection of

lab data will be obtained such as cultures glycosylated hemoglobin, hemoglobin and hematocrit, ESR, CRP and eGFR obtained per standard of care.
The normal group will have one time imaging and data collection. This group will have oral medical history taken and one set of images.

2) This will be performed at UT Southwestern Medical Center and Parkland with use of computer and Epic EMR system for chart review.

a. Data will be accessed at a secure UTSW or Parkland computer

b. Data collected will be stored on a UTSW computer secured network drive. The computer and the database are password protected.

c. Upon completion of data collection, the database will be completely de-identified of all PHI.

3) Statistical analyses to determine if these non-contact near-infrared non-invasive vascular imaging devices are able to provide information useful to healing, time to healing and complications such as requiring further surgery or more proximal amputation. Comparing differences within each individual patient outcome will be performed using IBM SPSS Statistics version 25 (IBM Corporation, Armonk, New York).

The instrument does not touch the patient and are being evaluated on their ability to predict wound healing. This is not standard of care, and is not being used to determine care.

4.b. List of the study intervention(s) being tested or evaluated under this protocol

x **N/A -** this study does not test or evaluate an intervention. Skip to item 4.d.

#	Study intervention(s) being tested or evaluated under the protocol *Add or delete rows as needed*	Affiliate Place a check next to institution(s) where the intervention will be performed	Local Standard Practice? Indicate whether the intervention is considered acceptable practice locally for applicable institutions
1		☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☐ Other: _____	☐ Yes
2		☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☐ Other: _____	☐ Yes
3		☐ UTSW	☐ Yes
		☐ PHHS	☐ Yes
		☐CMC	☐ Yes
		☐THR	☐ Yes
		☐TSRH	☐ Yes
		☐ Other: _____	☐ Yes

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4.c. Risk:Benefit Analysis of study interventions being tested or evaluated under this protocol

For each study intervention identified in section 6b above, complete a risk:benefit analysis table.

(Two tables are provided, copy & paste additional tables as needed or delete both tables if this study does not test an intervention)

5. Safety Precautions. *(Describe safeguards to address the serious risks listed above.)*

a. Describe the procedures for protecting against or minimizing any potential risks for each of the more than minimal risk research procedures listed above.

N/A not more than minimal risk

b. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse events, or unanticipated problems involving subjects.

Provided as standard of care.

c. Will the safeguards be different between/among groups?

☐ Yes ☑ No

No difference.