1) Protocol Title

a) **Incisional Negative Pressure Wound Therapy in High Risk Patients Undergoing Panniculectomy: A Prospective Randomized Controlled Trial** 10/25/2015

b) Chad M. Bailey, MD; Yunfeng, Xue, MD; Michael S. Wong, MD (PI)

2) IRB Review History

NA

3) Objectives

Aim: to evaluate benefits of PICO in high-risk panniculectomy patients in preparation for renal transplant.
Objectives: Evaluate wound healing complications and overall morbidity as well as scar quality and quality of life in high-risk patients who undergo panniculectomy in preparation for renal transplant with and without PICO therapy measuring the following endpoints:

1) Primary: wound healing complications
2) Secondary: drainage, hematoma, seroma
3) Tertiary: scar (Vancouver scar scale), pain (visual analog scale, narcotic use), quality of life (SF-36)

4) Background

Incisional negative pressure therapy (INPWT) has previously been shown in certain patient populations to decrease wound healing complications, decrease the rate of hematomas and seromas, as well as have better scar quality. We have found a group of patients, those who have panniculectomies in preparation for renal transplant, with significantly higher rates of wound healing complications (Bailey et al, Ann Plast Surg. 2015 May;74suppl 1:S9-11.). We believe the best way to demonstrate benefits of incisional negative pressure wound therapy will be in this group of patients known to have significantly higher rates of wound complications.

5) Inclusion and Exclusion Criteria

Inclusion criteria: All patients undergoing panniculectomy in preparation for renal transplantation at the University of California Davis Medical Center. Patients who are entered into the trial and have 30 days of follow up, and those in the INPWT study arm who successfully complete 7 days of treatment, will be included.

Exclusion criteria: All patients who previously demonstrated a hypersensitivity reaction to adhesives and qualify for panniculectomy in preparation for renal transplantation, or all patients who are undergoing panniculectomy for reasons other than in preparation for renal

transplantation (i.e. after massive weight loss or for cosmetic reasons). Patients who do not complete the duration of treatment of negative pressure wound therapy (7 days), or patients who do not follow up for a minimum of 30 days from the date of surgery will be excluded. Adults unable to consent, infants, children, teenagers, pregnant patients and prisoners will be excluded. It is also extremely unlikely, based on our study population, that we will encounter any of these patients.

6) Number of Subjects

We would ideally like to enroll 30 subjects. Data evaluation will begin after 10 subjects have enrolled and met inclusion criteria.

7) Recruitment Methods

All subjects will be patients of Dr. Michael Wong, and he will be the only attending surgeon of record for this study. Subjects will be asked by the principal investigators (Wong or Bailey) if they would like more information about the study during their preoperative visit. If they are interested, after they have qualified for panniculectomy in preparation for renal transplantation, the study can be discussed with them at their initial clinic visit, or they may elect to receive a phone call at a later time. No patients will be formally recruited outside of the preoperative discussion. There are no materials (paper or otherwise) that will be used to help recruit patients. No advertisements will be used. Identification of subjects will require access to personal health information without HIPAA authorization in that every patient who qualifies for a panniculectomy in preparation for renal transplantation qualifies.

8) Compensation to the Subjects

Subjects will not be compensated for this study

9) Study Timelines

The duration of an individual subject's participation will be at a minimum of 30 days from the date of surgery or from the date of their last related operation (additional operations required as a result of their panniculectomy). The duration of their inclusion in the study should be a maximum of 10 years to allow for adequate follow up, and to include wound healing after possible renal transplantation. The duration anticipated for enrollment will be up to 6 years. The estimated date of completion of the study will be July 2021.

10) Study Endpoints

Primary endpoints: Wound healing complications (separation, abscess, hematoma, seroma, cellulitis)

Secondary endpoints: Drainage of hematoma, seroma or abscess.

Tertiary endpoints: Scar (Vancouver Scar Scale), pain (visual analog scale, narcotic use), quality of life (SF-36).

11) Procedures Involved

We propose a prospective trial be performed where patients who are already selected to undergo panniculectomy in preparation for renal transplantation (who are inherently at high risk for developing wound healing complications) be treated with incisional negative pressure wound therapy in an effort to evaluate the effect of negative pressure wound therapy on wound healing complications. Patients will be randomized to participate after the patient qualifies for panniculectomy in preparation for renal transplantation. The surgeon will not be made aware of thtee randomization until after standard wound closure is performed. If a patient enrolls and is placed in the control group, they will receive standard of care operative incision treatment (dermabond/topical skin adhesive) after standard closure. If a patient is enrolled in the incisional negative pressure wound therapy arm, they will receive standard wound closure and incisional negative pressure wound therapy overlying. This device is placed on the wound, sterilely, in the operating room, to conclude the procedure. The incisional negative pressure wound therapy device is to remain in place for 7 days, and will be removed in clinic after completion. This device is the equivalent of an operative dressing, and is removed in the same fashion as any other dressing. If there are overt signs of wound healing complications, incisional negative pressure wound therapy will be discontinued immediately and the patient will be treated according to standard of care. If the patient removes the incisional negative pressure wound therapy device, either purposefully or accidentally, they will be switched to standard of care dressings. The incisional negative pressure wound therapy device will not be replaced on a wound for any reason, as the wound, once exposed after the operation, is rendered contaminated.

For the purposes of this study, the FDA approved PICO (Smith & Nephew) incisional negative pressure wound therapy will be used for all patients in the INPWT arm.

Data collection will be solely through EMR. The SF-36 (Short Form Health Survey) will be used to evaluate patient's quality of life during and after treatment with INPWT. All mailed forms to be filled out will include self addressed envelopes.

Baseline characteristics to be collected will include age, gender, race, BMI, diabetes, smoking status, renal failure cause, hypertension, pulmonary disease, vascular disease, prior abdominal operations, prior lower abdominal incisions, prior cesarean sections. Postoperative/long term follow up data to be collected will include wound healing characteristics including complications, additional antibiotic

administration, narcotic use, time to drain removal, scar quality (Vancouver Scar Scale), quality of life (SF-36), length of hospitalization, number of subsequent hospital visits, number of procedures related to postoperative wound management, and 30 day mortality of any cause.

No blood will be drawn for this study.

12) Data and Specimen Banking

No data or specimens will be banked for this study.

13) Data Management and Confidentiality

The association between patient with and without INPWT and postoperative complications will be evaluate overall and in subgroup analyses using univariate regression analysis. Means and standard deviations will be used to summarize continuous variables. Frequencies and proportions will be used to present the categorical clinical characteristics. Fisher's exact test will be used to test associations between complications and categorical variables. Univariate and multivariate logistic regression models will be used to analyze associations between complications and INPWT use. Univariate analysis will be used to evaluate the association between complications and other potential predictive factors (sex, age, BMI, smoking status, earlier abdominal surgery). A stepwise model selection method will be used to fit a multivariate logistic regression model after identifying variables by univariate logistic regression. A post-hoc power analysis will be performed.

Each patient included in the retrospective review will receive a study number. One key linking the patient medical record number to the study number will exist, and will be secured within the department of Transplant Surgery at the University of California, Davis. The key will only be available to the principal investigator, and will be terminated at the conclusion of the study. An electronic database will be generated from the patients' study number, age, and the data sets. The database will not contain patient identifiers such as name, address, dates, phone numbers, fax numbers, e-mail addresses, social security numbers, medical record numbers, health plan beneficiaries, biometric identifiers, or photographs. The proposed construct of our database nearly entirely de-identifies the protected health information with the exception of age. We recognize patient age is a potential identifier. However, the patients' ages may be a significant risk factor for wound complications, and thus will be included within the study. We will protect this information by only granting access to the study personnel listed above and maintaining the database on a single computer dedicated to this research study. We will not allow reproduction of the database. Protected health information will not be re-used or disclosed to any other person

or entity, except as required by law or for authorized oversight of the research project.

14) Provisions to Monitor the Data to Ensure the Safety of Subjects

This study involves no more than minimal risk to the subjects.

15) Withdrawal of Subjects

There are no anticipated circumstances where a patient will be withdrawn from the study. If a patient requests to have the INPWT device removed prior to completing 7 days of treatment postoperatively, the device will be removed and they will receive standard of care postoperative wound care and follow up. Purposeful or accidental discontinuation of the INPWT device by the patient prior to completing 7 days of treatment will not preclude the patient from continuing to participate in this study, as inclusion of their data will still be important to our study. Purposeful reason for discontinuation of the INPWT device does not include intentional removal by or at the direction of the physician or medical provider for any reason, as, again, these patient's data is still important for evaluation in our study. If a subject discontinues INPWT for any reason prior to completing 7 days of treatment, they will continue to receive standard postoperative care (wound care and follow up).

16) Risks to Subjects

Risks to the subjects are no more than minimal. The device works identically to a postoperative dressing, save for a small canister than can fit in the palm of a hand. This canister has previously been reported as either a non-issue or a minor nuisance by most patients. This is in contrast to requiring patients to perform standard of care dressing changes at home for soaking, which increases the risk of periwound irritation and/or blistering. Patients may also shower by removing the canister (electrical device), and replacing after.

There are no currently unforeseeable risks. There are no risks to an embryo or fetus should the subject be or become pregnant. There are no foreseen risks to others who are not subjects (i.e. health care providers, partners, family members, friends).

17) Potential Benefits to Subjects

Previous studies have demonstrated the likely benefit of incisional negative pressure wound therapy on high risk wounds (Conde-Green, et al. Ann Plast Surg. 2013 Oct;71(4):394-7. Stanard JP, et al. Ostomy Wound Manage. 2009 Aug 1;55(8):58-66. Atkins BZ, et al. Surg Innov. 2009 Jun;16(2):140-6). Specifically, the decreased rate of wound healing complications leading to expedited recovery, decreased use of antibiotics, decreased re-operation rate and possible improved scarring.

18) Vulnerable Populations

Pregnant women, prisoners, neonates, children and impaired adults are inherently not renal transplant candidates and will not be encountered in this study.

19) Multi-Site Research

NA

20) Community-Based Participatory Research

NA

21) Sharing of Results with Subjects

Relevant findings critical to the patient's future care will be shared via secure messaging (through EMR or through confidential transmission) to the patient's primary care provider. The results of the study will be made available to all physicians via literature publication at the conclusion of the study, however, no efforts will be made to individually communicate the results of the study to all participants, as contact information is frequently not adequately updated, sometimes unavailable and in situations where patients may be deceased.

22) Setting

All research will be conducted at the University of California, Davis Medical Center (Sacramento, CA). Patients will be recruited during their preoperative visit after they have been selected to undergo panniculectomy in preparation for renal transplantation. The application of the wound vac will occur in the operating room under sterile conditions after standard closure, concluding the operation. There is no necessary involvement by a community advisory board.

23) Resources Available

Research Coordinator (TBD): responsible for randomization of patients, ensuring device availability when applicable, will be available as an additional vector for postoperative communication with patients, will be jointly responsible for maintaining a prospective database regarding previously mentioned patient variables and outcomes.

Research Assistant (TBD): Will aid in data collection and evaluation, study design, manuscript production and editing.

Co-investigator (Chad M. Bailey, MD. Resident Physician): Responsible for study design, data collection and evaluation, manuscript production, editing and submission, and future presentations, if applicable. He will also be responsible for the supervision of the research coordinator and assistant(s). Dr. Bailey is an integrated plastic surgery resident at the University of California, Davis Medical Center, and has previously published the UC Davis experience in performing panniculectomy in

preparation for renal transplantation (please see prior reference). He has also served as the research assistant on two previous publications, on both of which he was responsible for confidential and secure data acquisition and evaluation.

Investigator (Michael S. Wong, MD. Professor of Surgery): Responsible for study design, data collection and evaluation, manuscript production, editing and submission. Will also be responsible for the supervision of the research coordinator and assistant(s). Dr. Wong is a Professor of Surgery in the Division of Plastic Surgery at UC Davis Medical Center, the Plastic Surgery Residency Program Director, and has published numerous manuscripts in the field of plastic surgery. He is also an active member of the American Association of Plastic Surgeons, the American College of Surgeons, the American Medical Association, the American Society for Reconstructive Microsurgery, the American Society of Plastic Surgeons, the California Society of Plastic Surgeons, and the University of California, Davis Surgical Society. He is the only surgeon at UC Davis to have performed panniculectomy in preparation for renal transplantation.

There is not expected to be any difficulty or shortfall in recruiting an adequate number of subjects during our proposed study time. Time devoted to conducting research during our allotted study period should average 1-2 hours per week. Facilities will be the UC Davis Plastic Surgery Clinics and Operating Rooms. Additional medical or psychological resources are very unlikely to be necessary as a result of this study.

All persons assisting with the research will attend a presentation explaining the study and the rationale for the study as well as an explanation of their role within the project. Furthermore, they will be required to complete online UC Davis HIPAA training and briefed again in regards to the appropriate handling of patient information.

24) Prior Approvals

This study has not been previously reviewed.

25) Provisions to Protect the Privacy Interests of Subjects

Subjects privacy interests and personal information will be protected through standard HIPAA practices, including reporting of confidential information only to the patient. Patients will have access to the Plastic Surgery clinic and research coordinator as well as on call Plastic Surgery staff unconditionally throughout the perioperative period, including, but not limited to, the period of time while the negative pressure wound therapy device is in place. Patients will be examined in accordance to our surgery clinic policy and with a chaperone when necessary. Only the research team and those providing direct care to the patient are permitted to access sources information about the subjects.

26) Compensation for Research-Related Injury

Patients will not be compensated

27) Economic Burden to Subjects

There is no obvious economic burden to patients participating in this study.

28) Consent Process

Patients will be approached about the study either at their preoperative clinic evaluation or by phone after their clinic evaluation, prior to their operation. Patients will be allowed to wait until the day of surgery to consent. Because of the short study period (7 days) there will be no process necessary to ensure ongoing consent. We will be following HRP-090.

Languages other than English that patient's may speak are numerous (e.g. Spanish, Mandarin, Tagalog, Japanese, etc). Consent will be obtained using a UC Davis approved interpreter in person. The written consent will be translated into the patient's language of preference by interpretive services. If the patient cannot achieve sufficient understanding of the study through the help of an interpreter, the patient will be excluded from the study.

No patients under the age of 18 years old will be included in the study.

Cognitively impaired adults are not candidates for renal transplantation and will not be encountered or included in this study. Also patients who cannot provide consent are not candidates for renal transplantation and will not be included in this study.

We will not be requesting a waiver of consent for this study.

29) Process to Document Consent in Writing

We will be following HRP-091. Please see attached document HRP-502. Our research presents no more than minimal risk of harm to subjects but does involve procedures (incisional negative pressure wound therapy dressing placement at the end of planned panniculectomy).

30) Drugs or Devices

PICO negative pressure incisional wound therapy is an FDA approved device already stored in the Pavilion operating room. The device comes sterilized, and there is no special handling of the device necessary beyond standard sterile technique. If the patient has been randomized into the study group, preoperative planning will include the assurance that the device is available for use prior to the operation. The operation is performed by a single surgeon at our institution, and thus will only be used by an authorized investigator.