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TITLE: Can Preoperative Skin Perfusion Predict Wound Healing Complications in High-Risk Peri-Articular Tibial Fracture Fixation

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CONTRACTING ORGANIZATION: University of Maryland, Baltimore, MD

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

This prospective single group observational study will enroll 160 patients with closed peri- articular tibial fractures that require surgical fixation from three trauma centers in the United States. Following informed consent, eligible patients will undergo LA-ICGA perfusion measurements of their injured limb at their index surgery as well as their delayed open definitive surgery (if required). The perfusion will be standardized relative to the capillary ICG concentration as measured by a pulse dye densitometer. Patients will be assessed at regular clinical follow-up visits for 90 days after definitive fixation and monitored for the primary outcome of wound complications.

15. SUBJECT TERMS

None listed.

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1. INTRODUCTION:

Using a commercially available LA-ICGA system to objectively measure soft-tissue perfusion, our proposed research continues the work from our pilot studies. The current study will establish the relationship between preoperative soft tissue perfusion and postoperative wound complications for periarticular tibia fractures. Additionally, the study will quantify the magnitude of perfusion recovery from the time of injury to definitive fixation when a delayed fixation strategy is selected.

2. KEYWORDS:

- **IRB –** Internal Review Board
- **HRPO –** Human Research Protections Office
- **DoD –** United states Department of Defense
- **UMD –** University of Maryland, Baltimore
- **DHMC** – Dartmouth-Hitchcock Medical Center
- **UCI** – University of California, Irvine medical center
- **LA-ICGA** – Laser Assisted Iodocyanine Green Angiography

3. ACCOMPLISHMENTS:

What were the major goals of the project?

- Draft, edit and submit protocol to University of Maryland, Baltimore IRB
- Submit protocol to HRPO
- Draft, modify and finalize case report forms (CRFs) for enrollment and follow-ups
- Build digital database for CRFs using UMD's REDCap
- Establish subcontracts between UMD, Dartmouth-Hitchcock Medical Center, and University of California Irvine
- Site Training and Professional Development
- Enrollment: 160 patients (across all sites; 120 UMB and ~40 DHMC/UCI)
- Achieve 100% primary outcomes at all patient follow-up timepoints
- Perform site monitoring and data validation
- Data collection, cleaning, validation and analysis (all sites)
- Manuscript preparation and other knowledge translation activities

What was accomplished under these goals?

Summary CY2 (Q1-Q3):

- University of Maryland received IRB approval for Protocol Version 1 and Case Report Forms. HRPO granted protocol number (**HP- 00093194**) in Q1.
- A REDCap database was built for data collection, management, and multi-site sharing.
- DHMC and UCI were approved as participating sites by the University of Maryland IRB. A reliance agreement between DHMC and UMD was approved and fully executed. Additionally, DHMC obtained local IRB approval, initiated project start up and began training new team members.
- UMD initiated subject recruitment and data collection in early February 2022. Enrollment: 10 subjects were recruited and in active follow-up at the end of Q2. The project achieved 100% primary outcomes at both the 2-week and 6-week patient clinical follow-up visits. *Note*: The primary outcome is to determine if preoperative skin perfusion is a predictor for post-op wound complications.

Summary CY2 (Q1-Q3 cont'd):

- Enrollment: 6 subjects were recruited in Q3. Total enrollment was 16 out of 120 subjects at the end of the quarter; 10 in active follow-up and 6 completed follow up at the 3-month timepoint. Primary outcomes were 100%, 92% and 75% at 2-week, 6-week and 3-month patient follow-up clinic visits, respectively. No patients reported unplanned surgeries, rehospitalizations, surgical site infections or other wound healing complications.

CY2 Q4:

- UMD continued subject recruitment, enrollment, and LA-ICGA data collection during Q4. Out of 34 patients screened; 24 were deemed ineligible, 4 refused and 6 provided consent / enrolled in the study. LA-ICGA perfusion measurements were collected on 6 subjects; 3 during definitive fixation only and 3 at index surgery + delayed open definitive fixations.
- To date, overall enrollment is 22 out of 120 subjects; 8 in active follow-up and 13 completed follow-up at the 3-month timepoint. Primary outcomes are 95%, 100% and 87% at the 2-week, 6-week and 3-month patient follow-up timepoints, respectively. No adverse events, complications, surgical site infections, unplanned surgeries or rehospitalizations were reported during follow-up clinic visits.
- Subaward contract extension with DHMC was finalized and approved.
- UCI reliance agreement and subaward contract was remitted and pending approval by UCI. UCI Informed consent documents were approved by UMD IRB. Submission to UCI local IRB is expected in the near future.

What opportunities for training and professional development has the project provided?

- UMD recruited and trained 3 new team members during Q3. All new team members obtained CITI Group 1 and 2 certifications and are proficient in patient screening, consent, enrollment, and LA-ICGA perfusion data collection / analysis, per the study protocol.
- DHMC initiated site training for its new team members in Q2 & Q3. Training activities will continue prior to patient enrollment.

How were the results disseminated to communities of interest?

- Data collection at UMD is currently in process. Preliminary results are only discussed amongst the Study Team. It is anticipated that results will be disseminated to communities of interest in the future.

What do you plan to do during the next reporting period to accomplish the goals?

By the next reporting time-point we expect:

- UC Irvine's informed consent document will receive local IRB approval.
- UCI will approve the subaward contract and fully execute the reliance agreement.
- All sites will have been trained on study procedures and granted access to the REDCap database.
- DHMC will have begun actively enrolling patients and initiated follow-ups.
- University of Maryland, Baltimore will continue patient recruitment, follow-ups and preliminary data analysis.
- UMD will remain in regular contact with participating sites to ensure these goals are accomplished in a timely and efficient manner and provide guidance to resolve challenges with site start-up.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

- It is anticipated this study will meet 100% primary outcomes at all clinic follow-up timepoints. As such, LA-ICGA may be useful in predicting post-operative wound complications.

What was the impact on other disciplines?

- To be determined once data collection and analysis is complete from all sites.

What was the impact on technology transfer?

- To be determined once this phase of the study is completed.

What was the impact on society beyond science and technology?

- It is anticipated that this study will determine if LA-ICGA is useful prognostic tool that surgeons can use to objectively guide their surgical decision making, specifically relating to the use of delayed fixation and optimal timing of definitive open fixation. The overarching goal is to minimize infection while safely expediting patient recovery and rehabilitation.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

- At this time, no changes in approach were deemed necessary.

Actual or anticipated problems or delays and actions or plans to resolve them.

- UCI has been delayed in overall project start-up and responsiveness in subcontracting and regulatory tasks. UMD must work closely with this site to resolve all challenges and develop timelines, goals and milestones to ensure future project success. UMD Site Coordinator and PI have discussed monthly check-in calls with UCI and newsletters to keep sites informed.

Changes that had a significant impact on expenditures

- No significant changes were made to impact expenditures.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

- No changes to report.

6. PRODUCTS:

- **Publications, conference papers, and presentations.** Nothing to Report
- **Journal publications.** Nothing to Report.
- **Books or other non-periodical, one-time publications.** Nothing to Report
- **Other publications, conference papers and presentations.** Nothing to Report.
- **Website(s) or other Internet site(s).** Nothing to Report
- **Technologies or techniques.** Nothing to Report
- **Inventions, patent applications, and/or licenses.** Nothing to Report.
- **Other Products.** Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	**Dr. Raymond Pensy**
Project Role:	Principal Investigator, UMD (Lead Site Protocol Chair)
Months Worked:	22
Contribution to Project:	Dr. Pensy provides overall project leadership and oversight.
Funding Support:	n/a

Name:	**Dr. Gerard Slobogean**
Project Role:	Co-Investigator, UMD
Months Worked:	22
Contribution to Project:	Dr. Slobogean provides on-going scientific and medical oversight.
Funding Support:	n/a

Name:	**LaShann Selby, MS, MPH(c)**
Project Role:	Clinical Research Coordinator, UMD (Lead Site POC)
Months Worked:	10
Contribution to Project:	Ms. Selby provides daily project oversight and management of study implementation (patient screening, enrollment, follow-up visits and data collection efforts). Maintains study documentation, case report forms, IRB applications and continuing reviews at lead site. Ms. Selby will provide site monitoring and data quality control to participating sites (UCI & DHMC).
Funding Support:	n/a

Name:	**Heather Phipps, MPS**
Project Role:	Clinical Research Specialist, UMD
Months Worked:	17
Contribution to Project:	Mrs. Phipps provided oversight on project start-up at the lead and participating sites, as well as IRB/HRPO and other regulatory matters at UMD.
Funding Support:	n/a

Name:	**Murali Kovvur**
Project Role:	Research Intern, UMD
Months Worked:	3 (Q3 – present)
Contribution to Project:	Mr. Kovvur participates in patient screening, enrollment, LA-ICGA data collection and patient follow-ups.
Funding Support:	n/a

Name:	**Joshua Lawrence**
Project Role:	Research Intern, UMD
Months Worked:	3 (Q3 – present)
Contribution to Project:	Mr. Lawrence participates in patient screening, enrollment, LA-ICGA data collection and patient follow-ups.
Funding Support:	n/a

Name:	**Kristin Turner**
Project Role:	Research Intern, UMD
Months Worked:	3 (Q3 – present)
Contribution to Project:	Ms.Turner participates in patient screening, enrollment, LA-ICGA data collection and patient follow-ups.
Funding Support:	n/a

Name:	**Kathleen Healey**
Project Role:	Research Intern, UMD
Months Worked:	7 (Q1-Q3)
Contribution to Project:	Ms. Healey participated in patient screening, enrollment, LA-ICGA data collection and patient follow-ups.
Funding Support:	n/a

Name:	**Natasha McKibben**
Project Role:	Research Intern, UMD
Months Worked:	5 (Q1-Q3)
Contribution to Project:	Ms.McKibben participated in patient screening, enrollment, LA-ICGA data collection and patient follow-ups.
Funding Support:	n/a

Name:	**Cole Zingas**
Project Role:	Research Intern, UMD
Months Worked:	5 (Q1-Q3)
Contribution to Project:	Mr. Zingas participated in patient screening, enrollment, LA-ICGA data collection and patient follow-ups.
Funding Support:	n/a

Name:	**Dr. Leah Ida Gitajn**
Project Role:	Co-Investigator, DHMC
Months Worked:	n/a
Contribution to Project:	No change to report. Dr. Gitajn is prepared to contribute to the study once the subcontract is finalized and site training has been completed.
Funding Support:	n/a

Name:	**Dr. John Scolaro**
Project Role:	Co-Investigator, UCI
Months Worked:	n/a
Contribution to Project:	No change to report. Dr. Scolaro is prepared to contribute to the study once the subcontracts, reliance agreements, and IRB/HRPO approvals are in order
Funding Support:	n/a

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

- No changes in support of PI or other senior/key personnel were made during this contract year.

What other organizations were involved as partners?

- DHMC and UCI have agreed to support the project by enrolling and following 40 participants. DHMC has received UMD and local site IRB approvals to begin study procedures. UCI must seek local IRB approval of their informed consent document prior to initiating study procedures.
    - **Organization Name:** (1) University of California at Irvine Medical Center; (2) Dartmouth-Hitchcock Medical Center
    - **Location of Organization:** (1) Orange, California; (2) Lebanon, New Hampshire
    - **Partner's contribution to the projec**t
        - **Collaboration**- Partner sites are expected to contribute to this project in the near term. It is highly anticipated that DHMC will initiate their processes in CY23 Q1, and UCI therafter.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Nothing to Report.

QUAD CHART: Updated to reflect CY 20 – CY22 Q4. Submitted as a separate document.

9. APPENDICES: Nothing to Report.