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**TITLE:** Optimizing Surgical Debridement Following High-Energy, Open Trauma with Dynamic, Contrast-Enhanced Fluorescence imaging

**PRINCIPAL INVESTIGATOR:** Ida Leah Gitajn, MD

**CONTRACTING ORGANIZATION**: Dartmouth-Hitchcock Medical Center, Lebanon, NH

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**PREPARED FOR:** U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

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Optimizing Surgical Debridement Following High-Energy, Open Trauma With Dynamic, Contrast-Enhanced Fluorescence imaging

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**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**
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**8. PERFORMING ORGANIZATION REPORT NUMBER**

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**13. SUPPLEMENTARY NOTES**

**14. ABSTRACT**
The proposed study will enroll 180 patients with open fractures to determine whether bone perfusion parameters, as measured by indocyanine green (ICG)-based Dynamic Contrast Enhanced Fluorescence Imaging (DCE-FI), is a predictor of unplanned all-cause reoperation as defined by the Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network reporting criteria. We will also modify and optimize the existing DCE-FI system for bone perfusion imaging in austere environments and/or forward operating units. This study represents the next important step towards optimizing surgical management of high-energy traumatic injuries, particularly in medical units supporting soldiers in battle. This will transform the current paradigm by providing military trauma surgeons with accessible tools that can be used by surgeons at any level of experience to objectively inform surgical debridement. In turn, this technique will directly improve patient outcomes after traumatic injury by reducing infection and complications requiring unplanned reoperation.

**15. SUBJECT TERMS**

| 16. SECURITY CLASSIFICATION OF: | | | 17. LIMITATION OF ABSTRACT | 18. NUMBER OF PAGES | 19a. NAME OF RESPONSIBLE PERSON |
|---|---|---|---|---|---|
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| Unclassified | Unclassified | Unclassified | Unclassified | 14 | 19b. TELEPHONE NUMBER *(include area code)* |

## TABLE OF CONTENTS

## 1. INTRODUCTION:

The focus of this prospective observational study is to (1) establish the range and variation associated with bone/soft tissue perfusion in patients with an open fracture, using ICG fluorescence imaging; (2) examine the relationship between perfusion and complications such as surgical site infection (SSI), persistent SSI, and fracture nonunion; (3) to determine whether the quantitative ICG fluorescence can be used to guide bony debridement in the setting of open fracture or infected fracture to minimize complications. A Pulse Dye Densometer, similar to a pulse oximetry probe, will be placed on the patient's finger to acquire an arterial blood input function during ICG injection. After exposure but prior to debridement, 0.1 mg/kg ICG will be injected intravenously. Video rate ICG fluorescence images will be acquired 20 seconds before and 4 minutes after ICG injection. The pulse dye densometer collects data on the ICG injection parameters so that the kinetic curves can be normalized to injection-related differences. The ICG dye is indirectly activated and the dynamic fluorescence due to bone perfusion can be captured by a video rate imaging system. Subjects will be followed for 1 year following the date of their fracture to report outcome data.

## 2. KEYWORDS:

AIF: arterial input function

BWH: Brigham and Women's Hospital

CDC: Centers for Disease Control and Prevention

CRF: Case Report Forms

DCE-FI: Dynamic Contrast Enhanced Fluorescence Imaging

DoD: US Department of Defense

DHMC: Dartmouth Hitchcock Medical Center

FI: fluorescence imaging

GCP: Good Clinical Practice

ICG: Indocyanine Green

ROI: Region of interest

SSI: Surgical Site Infection

STC: R Adams Cowley Shock Trauma Center

UMDB: University of Maryland Baltimore

UCI: University of California Irvine

## 3. ACCOMPLISHMENTS:

**What were the major goals of the project?**

Aim 1: Identify fluorescence imaging parameters using ICG-based DCE-FI that are associated with unplanned reoperation following high energy open fracture.

1a. Acquire ICG-based DCE-FI data in patients with open fracture (months 1-36)

- Perform intraoperative DCE-FI of patients with open fracture in 180 patients. 45 patients will be enrolled at site 1, 90 in site 3 and 45 at site 4 with 12 month follow-up.
- Complete data processing and determine associative relationships between simple post-debridement bone perfusion variables and unplanned reoperation.
- Develop a conversion algorithm

1b. Develop a human bone-specific kinetic hemodynamic model and evaluate the association between model-derived parameters and unplanned reoperation (months 13-48).

1c. Assess the association between injury-specific variables, demographic variables and comorbidities with both bone perfusion parameters and with unplanned reoperation (months 13-48).

1d. Apply machine learning techniques to identify kinetic curve-related parameters that are most strongly associated with unplanned reoperation (months 13-48).

**Milestones:**

• Successful imaging in 180 participants with open fracture. (image 60 participants each year of year 1-3)

• Establish a bone specific modeling to evaluate the association between model-derived parameters and unplanned reoperation. (years 2-4)

• Identify the best indicator for the bone that will have complication. (years 3-4)

Publication on the bone modeling, imaging, data analysis, etc (Journal of Bone and Joint Disease and J Biomed Optics) (1 or more publications each year)

• File provisional patent application with Tech Transfer Office based upon the bone modeling, ICG-Based DCE-FI for imaging guide orthopedic surgery ( years 2-4)

Aim 2: Modify, optimize and test the existing in-house developed ICG based DCE-FI system for bone perfusion imaging in austere environments and/or forward operating units close to the battlefield .

2a. Optimize and test the compact system for imaging austere environments (months 13-48)

• Optimize the compact system for austere environments and/or forward operating units close to the battlefield

• Test the system's performance, stability, rigidness for long distance travel.

• Compare the intraoperative performance with conversational imaging system (SPY Elite).

2b. Package and customize software for streamlined use and real-time data analysis in the operating room (months 13-48).

**Milestones:**

• Accomplish MatLab code for transferring video data, analysis imaging data with different model driven variables, overlaying fluorescence and white light images. (years 1-2)

• Demonstration of the software can perform the guidance to the debridement. (year 3)

• New compact system has the similar or better sensitivity, specificity, accuracy and stability for intraoperative DCE_FI , compare to SPY Elite. (year 3)

• Publication on the software and system (J. biomedical Optics et al) (1 or more publications each year of years 2-4)

• File addendum to full patent application with Tech Transfer Office based upon outcome data (year 4)

**What was accomplished under these goals?**

In the first quarter, our work was focused on a) submitting the protocols for institutional IRB approval; b) developing the procedures of patient imaging and data uploading, and training the clinical coordinators of all sites to ensure the imaging quality; c) imaging eligible patients at Dartmouth-Hitchcock Med. Center (DHMC); and d) improving the imaging data processing. In the second quarter, our work was focused on a) Continuation of the IRB protocol submission process and correspondence (b) Further developing analytical software and user interface /user experience (UI/UX) to allow the surgeon to annotate the surgical images right after the ICG-based DCE-FI in the surgical room (c) Continuing to image eligible patients at Dartmouth-Hitchcock Medical Center (DHMC) ; and (d) Improving image visualization. In the third quarter, our work was focused on a) Continuation of the IRB protocol submission process and correspondence with Brigham and Women's Hospital and University of California, Irvine (b) Receiving IRB and HRPO approval to begin recruitment at University of Maryland, R. Crowley Shock Trauma (c) Developing second generation of the arterial input function (AIF) device for improving the stability, sensitivity and easy accessibility. (d) Continuing to image eligible patients at Dartmouth-Hitchcock Medical Center (DHMC) and begin imaging eligible patients at University of Maryland, R. Cowley Shock Trauma, (e) Analysis the patient data using machine learning, and (f) Technical design to modify the existing in house developed ICG based DCE-FI system for bone perfusion in austere environments and/or forward operating units close to the battle field.

The specific objectives of this project are to: (1) study the relationship between bone perfusion and complications such as surgical site infection (SSI), and fracture nonunion and (2) to develop intraoperative hardware and software tools that are optimized for assessment of bone and soft tissue devitalization and for use in austere environments to provide critical intraoperative data which will inform surgical debridement.

During the first quarter protocols and informed consent forms were submitted to and approved by DH-H IRB for DHMC and processes continued to work towards site ceding for the 3 relying sites. The procedures for imaging patients, data uploading and training of the clinical coordinators at sites was developed in order to ensure consistency in the use of the SPY Elite and AIF system. As we were aware of from other projects, imaging processing time is one of the most important keys to utilize imaging guide surgery. Since ICG-based DCE-FI is based on analyzing a time sequences including more than thousand images, the processing time of image loading, fitting (to our specific bone perfusion mode, and display was up to about 20 minutes, depending on the laptop processing time. For overcoming this problem, we developed the new image processing code based on python. By utilizing Pydicom, Numpy, Scipy, and Imresize packages with python multiprocessing package, the processing time was improved from 20 minutes to 57 seconds, with 4 processes running parallel on a two-core laptop.

In the second quarter, Study protocols were submitted to the institutional IRBs at R. Crowley Shock Trauma, The University of California, Irvine and Brigham and Women's Hospital (BWH). The Engineering team worked on further development of analytic software and user interface / user experience to allow the surgeon to annotate the surgical images directly after the ICG based DCE-FI in the surgical room. Figure 1 is the illumination of our patient imaging workflow. We are using Stryker's Spy Elite to carry out ICG-based DCE-FI. As shown in Fig.1, the wavelength of the excitation light is 805 nm and the fluorescence light over the wavelength of 810nm will be detected by a CCD camera. Working distance is fixed on 30 cm and the size of the field of view is about 14x22 cm. For eliminating effects of ICG injection dose, injection rate, physiologic dispersion, and intravenous tubing volume on the shape and magnitude of the dynamic ICG curves, we are using a pulse dye densitometry clip on the patients' finger to obtain the subject-specific arterial input function (AIF). During the surgery, the surgeon sees real time overlay, white-light and fluorescence images. After the surgery, Kinetic analysis on each pixel is carried out and maps of kinetic parameters are obtained. Also during the second quarter, it was determined that the MATLAB code was too computationally demanding to be run on the tablets brought into the surgical room for measuring AIF and recording the surgical information. To overcome this problem, a new GUI based on Python was developed during quarter 3.

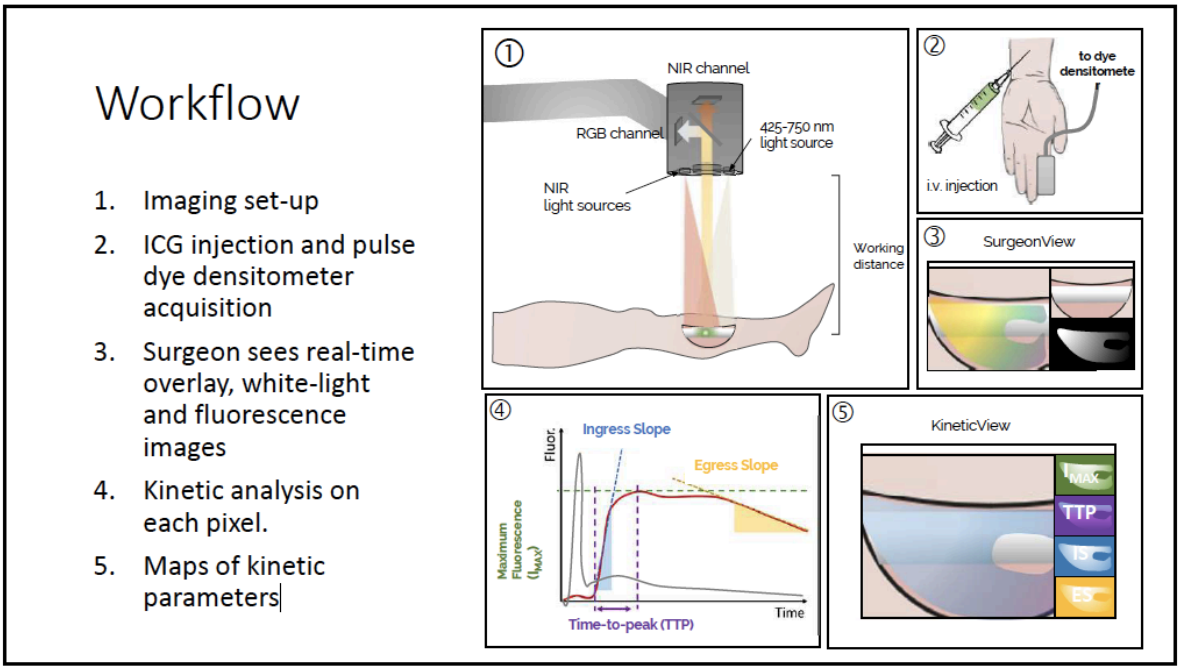


***Figure 1*** *Illumination of our patient imaging workflow*

Also in quarter 2, a better color overlay scheme was developed to improve imaging display, this in turn will better assist the surgeon in utilizing the imaging to guide debridement. For better control, a pig tibia fracture model. Figure 2 shows the updated kinetic parameter maps of a pig tibia under three different conditions. These conditions represent different levels of the damage to bone blood flow. In Fig.2,the left column shows the tibia without damage and with normal bone blood flow. The center column is after a 3 cm center bone segment has been removed to mimic the bone with neither endosteal nor periosteal blood flow. The right column shows the surface soft tissue from the proximal half of the tibia post stripping to mimic the damage in periosteal blood flow. The map of the total bone perfusion in the middle column clearly shows that the perfusion decreased significantly in the bone segment that was removed from the tibia, while the distal and proximal segments of the bone still have a similar level of the perfusion as shown in the left column. After the periosteal blood supply was damaged by stripping of the soft tissue, total bone perfusion was reduced significantly in the proximal end of the tibia, compared to that in distal end. (right column). A similar trend can be seen in other maps. For the purpose of improving the diagnostic power of differentiating injured bone from normal bone, we applied support vector machine analysis which generated a boundary between injured and normal bone, using kinetic perfusion variables (total bone perfusion and early perfusion fraction) (Figure 2). The damaged bone area (red) has been clearly separated from the normal bone area (green). More advanced SVM implementations are also being explored to leverage developments in computer vision in this area, including the concept of in-painting and regularization that provides a spatial component to the cost function. This will result in more natural and realistic boundary definitions free from fragmentation or artifacts.

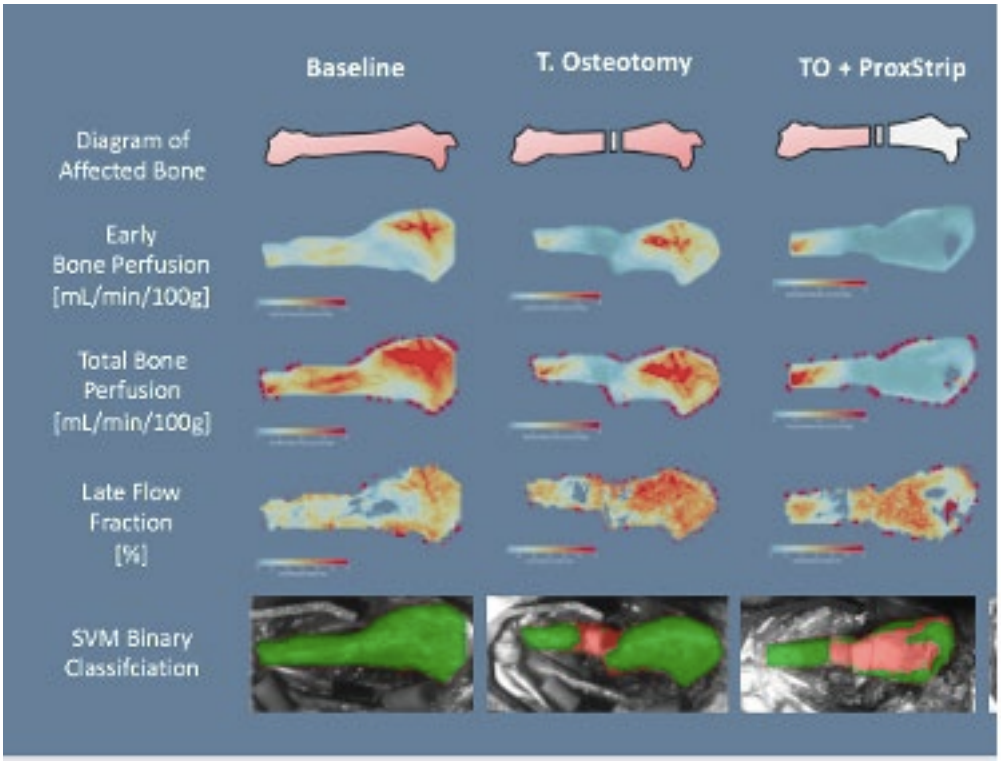


***Figure 2*** *the updated kinetic parameter maps of a pig tibia under three different conditions that represent different levels of the damage of bone blood flow.*

In the third quarter, our work continued to focus on the IRB protocol submission process and correspondence with Brigham and Women's Hospital; and University of California, Irvine. HRPO approval to begin recruitment at University of Maryland, R. Crowley Shock Trauma. Eligible patients continued to be enrolled at Dartmouth-Hitchcock Medical Center and imaging began at University of Maryland, R. Crowley Shock Trauma.

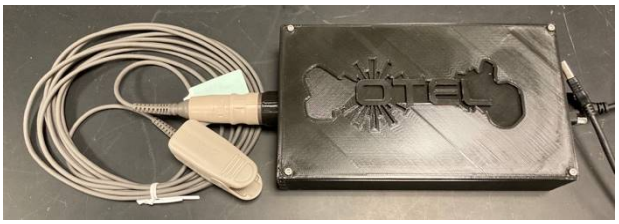

*Figure 3 Photo of the second generation of AIF device.*

Development also progressed on a second generation of arterial input function (AIF) device. The second generation seeks to improve stability, sensitivity and overall ease accessibility. Work continued on the technical design to modify the existing in house developed ICG based DCE-FI system for bone perfusion in austere environments and/or forward operating units close to the battle field. The effects of varying the indocyanine green injection dose, injection rate, physiologic dispersion of dye, and intravenous tubing volume propagate into the shape and magnitude of the arterial input function (AIF) during intraoperative fluorescence perfusion assessment, thereby altering the observed kinetics of the fluorescence images in vivo. For improving the sensitivity and stability of the AIF measurement device, we have developed a new generation of the AIF device which, based on the Texas Instruments Analog Front-End (AFE4490) integrated into an Arduino shield (PC-MED-0405, Protocentral). The benefit of using a breakout board rather than the TI evaluation board is that it can be addressed using an Arduino using the Serial Peripheral Interface (SPI). Through SPI the Arduino transmits and receives red and infrared signals measured by the 4490 and this can be transmitted to any device (PC, Tablet) using USB through custom-built Python software. Using python software to directly interact with the AFE4490 allows real-time visualization and streamlined UI/UX for saving data and processing AIFS> Figure 3 shows a photo of this new device. By using this new device, the raw data of the time-dependent concentration of ICG in the arterial system can be acquired by the pulse oximeter clipped on the patient finger, and then transferred into a Microsoft Surface Laptop for processing AIF.

In the fourth Quarter, both DH-H IRB and HRPO approvals were received to begin enrollment at Brigham and Women's Hospital. Forward progress continued with University of California, Irvine on approval through DH-H IRB and submission to HRPO is currently pending. As far as technical development is concerned, we have made four sets of AIF devices and compared the old and new AIF devices intraoperatively. Figure 4 is the raw data (a) and processed AIF curve (b) obtained from both the old and the new AIF devices. Figure 4 the raw data (a) and processed AIF curve (b) obtained from both old and new devices. The data obtained by the old and new devices are represented in blue and orange, respectively. It can be seen clearly that the raw data and produced AIF curves are almost an identical match to each other. The new AIF device is more reliable, stable, and simpler to use in the operating room.

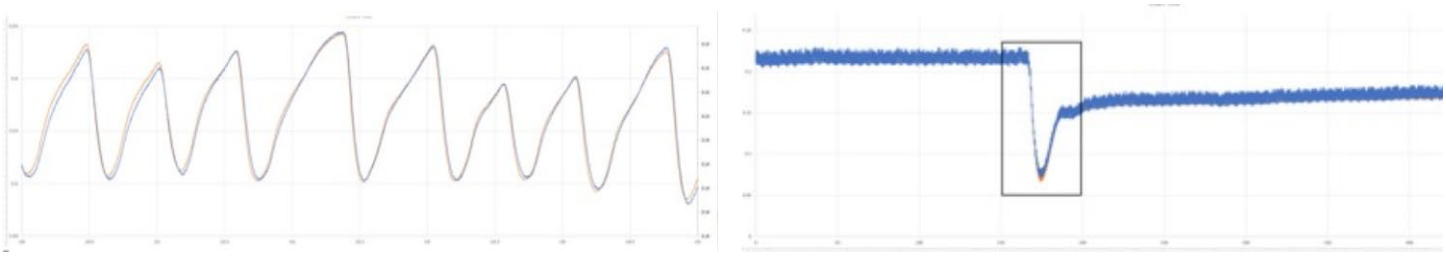


*Figure 4 the raw data (a) and processed AIF curve (b) obtained from both old and new devices. The data obtained by old and new devices represented in blue and orange, respectively.*

Since blood leaking from the bone and surrounding tissues of the surgical incision may cause artifact during the bone perfusion assessment during the 4 minutes of the ICG image acquisition, the surgeon suctions blood occasionally from the surgical area. In order to reduce the noise on the dynamic curves, due to the small motion effect of the region of interest (ROI) caused by the suctioning, we have developed an imaging processing software code to remove this motion effect. In this imaging processing, the images were registered by maximization of mutual information (MI), which can be applied to measure the statistical dependence between

the intensities of two images, move around the pixels to force them geometrically aligned. Figure 5 shows the images and dynamic curves of an open surgery patient before and after removing the motion effect. The patient is a 32 year old who suffered an open ankle fracture. Fig 5(a) and (b) are white light and the corrected ICG image at105 seconds, and Figure 5 (c) shows the corresponding ICG dynamic curves of ROIs in bone ( red) and skin (blue) areas. As shown in Fig.5 (c), The corrected curves (dark blue and red ) successfully corrected the motion effect shown in the original curves (light bule and yellow).

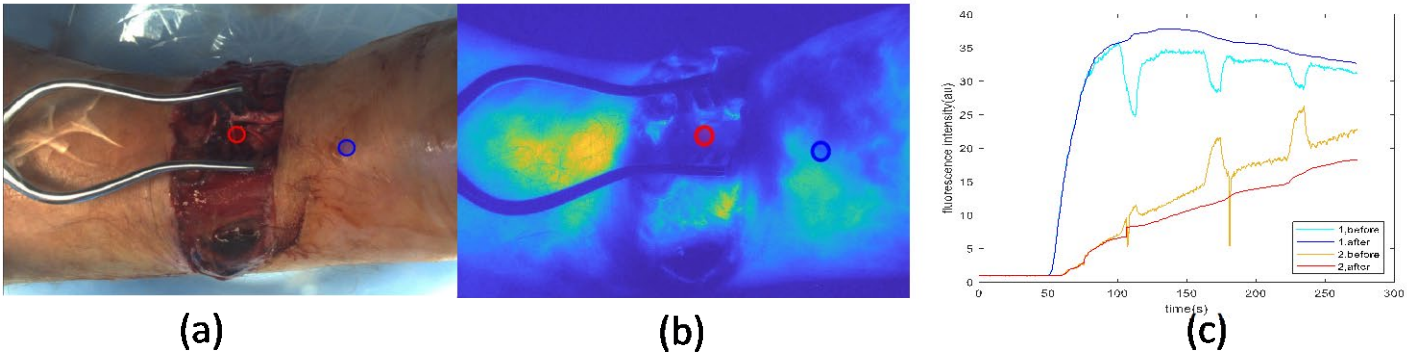


*Figure 5 Images and dynamic curves of an open surgery patient before and after removing the motion effect. (a) white light image of surgical view; (b) corrected ICG image at 105 seconds. Circles are the regions of the interest in bone (red) and skin (blue) area for testing the motion effects removal; and (c) the corresponding ICG dynamic curves of ROIs in bone ( red) and skin (blue) areas, before (light blue and yellow) and after (dark blue and red) the correction.*

Figure 6 is an example of the images and DCE-FI curves for an open surgery patient. This is a 44 year old male patient with a left open tibia / fibula fracture Fig.6 (a) and (b) are white light and ICG image at 250 seconds of the surgical field. (c) is DCE-FI curves at each of 5 ROIs that represent non-significantly damaged/healthy bone area (pink and yellow), significant damaged area (light blue and red) and normal skin area (green and dark blue); and (d) and (e), bar graphs of maximum intensity of ICG and the initial increase rate (IS) of the dynamic curves. Comparing to the significantly damaged ROIs, Imax and IS are significantly higher in non-significantly damaged/healthy ROIs, while the two reference skin ROIs are very similar.

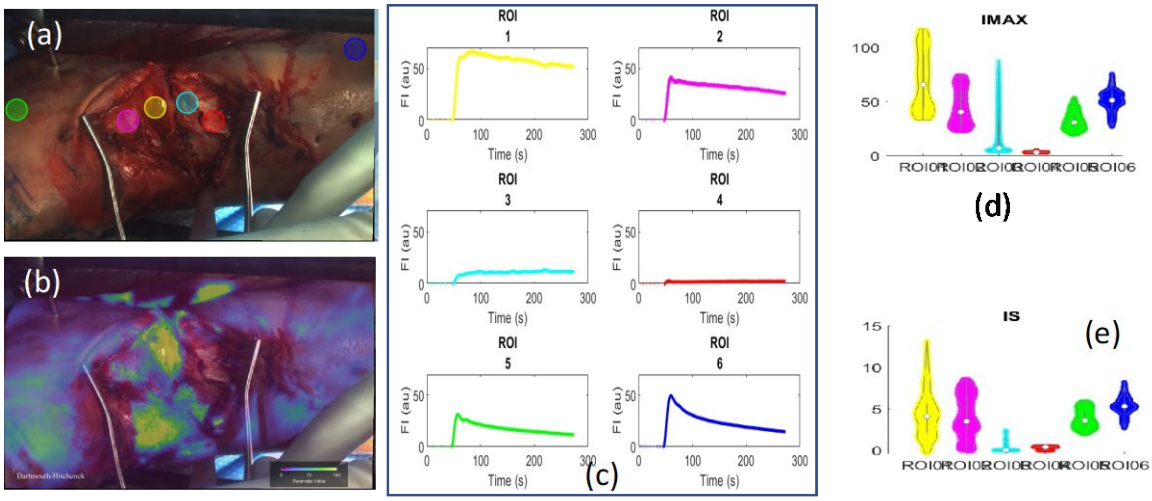


*Figure 6 an example of the images and DCE-FI curves for an open surgery patient. (a) and (b) white light and ICG image at 250 s of the surgical field; (c) DCE-FI curves at each of 5 ROIs that represent non-significant damaged/healthy bone area (pink and yellow), significant damaged area (light blue and red) and normal skin area (green and dark blue); (d) and (e), bar graphs of maximum intensity of ICG and the initial increase rate (IS) of the dynamic curves of 5 ROIs.*

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

Nothing to Report

**How were the results disseminated to communities of interest?**

Nothing to Report.

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

In order to accomplish the goals of this project we will continue to work on getting the final site University of California, Irvine IRB approved. We are currently scheduling start up meetings with both BWH and UCI so that they can begin imaging eligible patients. We will continue to image patients as well as collect follow up data on patients at both DHMC and Shock Trauma. To date 26 patients have been imaged at DHMC and 2 at Shock Trauma.

We are continually working on the improvement of the patient image process, towards the real time imaging display in the surgical room to guide orthopedic surgery, we will focus on developing a compact ICG-sensitive, DCE-FI system for bone perfusion imaging in austere environments and/or forward operating units close to the battlefield. Based on our existing imaging system for dynamic Cherenkov light imaging during radiation treatment, we have developed a protocol type imaging system and LED light source for ICG based DCE-FI. Figure 7 shows the photos of compact camera (a) and the home made LED sources (b) for this system. This is a time gated imaging system for eliminating the ambient light effect in austere environments and very compact, allowing it to be carried into the forward operating units close to the battlefield. We will modify, optimize and test this protocol type system and validate it intraoperatively in the surgical room.

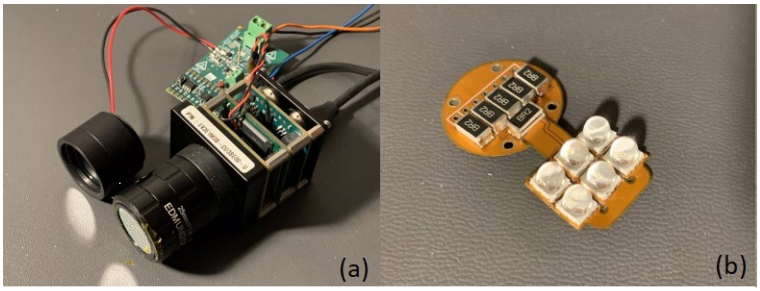


*Figure 7 Photos of (a) compact camera and (b) the home made LED sources for a compact DCE-FI system.*

## *4.* IMPACT:

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

Optimization of AIF device and integration into analytic pathway is critical to allow more nuanced analysis of ICG-based data, including inflow and outflow parameters, which clearly differ across normal and diseased states (which is a substantial advancement beyond the maximum intensity images currently available on the commercial ICG-based fluorescence devices). Development of standardized analytic tools is also critical to improve and optimize visualization of data in the operating room. All of these technical developments will clearly improve the quality and quantity of data derived from ICG-based fluorescence imaging as well as the presentation of this data to surgeons in the operating room. This is expected to have a profound impact on the overall utility of this intraoperative imaging tool.

We anticipate that the overall findings of this study will demonstrate the relationship between several bone perfusion-based variables and clinically important complications which will profoundly impact treatment of

severe open fractures by providing surgeons with a new intraoperative tool that provides clinically relevant data around healing potential and risk of infection.

**What was the impact on other disciplines?**
This research may impact other fields that require assessment of bone health or bone perfusion, such as oral and maxillofacial surgery (specifically with regards to evaluation of conditions such as osteonecrosis of the jaw as well as fracture healing/bone infection) as well as plastic surgery (assessment of free flaps that involve bone such as free fibula among others).

**What was the impact on technology transfer?**
Nothing to Report.

**What was the impact on society beyond science and technology?**
Nothing to Report.

## 5. CHANGES/PROBLEMS:

**Changes in approach and reasons for change**
Nothing to Report

**Actual or anticipated problems or delays and actions or plans to resolve them**
Due to the COVID-19 pandemic, our work in the first quarter mainly focused on the activities that could be accomplished remotely and the numbers of the patients enrolled in the study was delayed. In order to increase recruitment numbers, and reach our enrollment goal, we added an additional site, BWH, into the study. To date, as a result of COVID as well as unanticipated challenges with using a single central IRB (as opposed to each site using individual IRBs) we are behind on patient enrollment. However, with three sites plus the primary site expected to be enrolling by the first quarter of year 2 we expect the patient numbers to increase significantly.

**Changes that had a significant impact on expenditures**
Nothing to Report

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

**Significant changes in use or care of human subjects**
Nothing to Report

**Significant changes in use or care of vertebrate animals**
Nothing to Report

**Significant changes in use of biohazards and/or select agents**
Nothing to Report

## 6. PRODUCTS:

- **Publications, conference papers, and presentations**

**Journal publications.**

Elliott JT, Addante RR, Slobegean GP, et al. Intraoperative fluorescence perfusion assessment should be corrected by a measured subject-specific arterial input function. *J Biomed Opt* 2020; 25: 1-14. 2020/06/11. DOI: 10.1117/1.JBO.25.6.066002.

Gitajn IL, Slobogean GP, Henderson ER, et al. Perspective on optical imaging for functional assessment in musculoskeletal extremity trauma surgery. *J Biomed Opt* 2020; 25 2020/09/02. DOI: 10.1117/1.JBO.25.8.080601.

**Books or other non-periodical, one-time publications.**

Nothing to Report

**Other publications, conference papers and presentations**.

Gitajn IL, Jiang S, Henderson E, Slobogean G, O'Hara N, Scoalro J, Pogue B, Elliott J. Optimizing Debridement using ICG-based Fluorescence Imaging. Orthopaedic Trauma Association Annual Meeting, 2020

Gitajn, I. Leah, Han, X., Elliott, J.T., Cao, X., Christian, M. L., Chockbengboun, T., Henderson, E. R., and Jiang, S.," Intraoperative Indocyanine Green-based dynamic contrast-enhanced fluorescence imaging can effectively quantify bone perfusion," *Annual meeting of Society of Military Orthopedic Surgeons,* ***Abstract submitted*** (2021).

Han, X., Demidov, V., Gitajn, I.L., Jiang, S., Elliott, J.T., "Intraoperative assessment of patient bone viability using texture analysis of dynamic contrast-enhanced fluorescence imaging," in European Conference on Biomedical Optics (ECBO) (2021), paper 3565356. (in press)

Han, X., Demidov, V., Wirth, D., Byrd, B., Davis, S.C., Gitajn, I.L., Elliott, J.T., "Validation of dynamic contrast-enhanced bone blood flow imaging technique with fluorescent microspheres," in SPIE Photonics West (2022), paper BO111-7. (in review)

Jiang, S., Elliott, J.T., Xin, J., Cao, X., Yu, X., Han, X., Christian, M. L., Henderson, E. R., Pogue, B. W. , and Gitajn, I. Leah " ICG-based dynamic contrast-enhanced fluorescence imaging guided open orthopaedic surgery—pilot patient study," *SPIE Photonics West* 11625-19 (2021).

- **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: Ida Leah Gitajn, MD
Project Role: Principal investigator (DHMC)
Researcher Identifier: 0000-0001-8649-7385
Nearest person month worked: 9
Contribution to Project: No Change

Name: Eric R. Henderson, MD
Project Role: Sub-Investigator (DHMC_
Researcher Identifier: 0000-0002-0371-010X
Nearest person month worked: 9
Contribution to Project: No Change

Name: Melanie L. Christian
Project Role: Lead Research Coordinator (DHMC)
Researcher Identifier: 0000-0001-6971-8844
Nearest person month worked: 9
Contribution to Project: No Change

Name: Theresa Chockbengboun
Project Role: Research Coordinator-(DHMC)
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No Change

Name: Logan Bateman
Project Role: Research Coordinator-(DHMC)
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: Logan has completed case report forms and aided in obtaining subject imaging in the operating room. He has also aided in reporting as instructed by the principal investigator.

Name: Jonathan T. Elliott
Project Role: Scientist / Data Analyst
Researcher Identifier: 0000-0002-8485-0234
Nearest person month worked: 9
Contribution to Project: No Change

Name: Shudong Jiang
Project Role: Scientist / Data Analyst
Researcher Identifier: 0000-0001-7396-7886
Nearest person month worked: 9
Contribution to Project: No Change

Name: Xu Cao
Project Role: Scientist / Data Analyst
Researcher Identifier: 0000-0002-8749-1716
Nearest person month worked: 9
Contribution to Project: No Change

Name: Thomas Usherhill
Project Role: Engineer
Research Identifier:
Nearest person months worked: 9
Contribution to Project: No Change

Name: Yue Tang
Project Role: Scientist / Data Analyst
Researcher Identifier:

Nearest person month worked: 9
Contribution to Project: No Change

Name: Xinyue Han
Project Role: Scientist / Data Analyst
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No Change.

Name: Gerard Slobogean
Project Role: Site Investigator – R. Crowley Shock Trauma
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No Change

Name: Joshua Rudnicki
Project Role: Research Team Member (R. Crowley)
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No change

Name: Michael Weaver, MD
Project Role: Site Investigator – Brigham and Women's Hospital
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: Dr. Weaver has performed all responsibilities of the site investigator for pre start-up activities

Name: Abigail Sagona
Project Role: Research Coordinator Brigham and Women's Hospital
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: Abigail has aided in ceding review between Brigham and Women's Hospital and DHMC and creation of site specific documents as well as other study start up tasks that are site specific.

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

Nothing to Report

**What other organizations were involved as partners?**
**Dartmouth College, Thayer School of Engineering**
**14 Engineering Drive**
**Hanover, NH 03755**

## 8. SPECIAL REPORTING REQUIREMENTS

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:** See attached Quad Chart.

**9. APPENDICES:** See attached copy of journal articles and Quad Chats.