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

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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**

NONE LISTED

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**Prescribed by ANSI Std. Z39.18**

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## 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:

*The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

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

*List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.*

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?**

*For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.*

*1) Major activities*

In the nineth quarter, our work was focused on a) Enrollment at DHMC, University of Maryland, University of California and Brigham and Women's hospital, as well as completing patient follow up visits; (b) Continuing to work imaging data process procedure to eliminate the surface blood (out of bone) and (c)

Continually working on developing and validating the compact bone perfusion imaging system (cBPI) for bone perfusion in austere environments and/or forward operating units close to the battle field.

In the tenth quarter, enrollment remained continually delayed by the COVID-19 pandemic, but had totally 73 patients with open extremity fractures who underwent surgery at DHMC were successfully enrolled and imaged in this study. We continually working on analysis imaging data to predict unplanned reoperation and infection following high energy open fracture, and developing and validating the compact bone perfusion imaging system (cBPI) for bone perfusion in austere environments and/or forward operating units close to the battle field.

In the eleventh quarter, our work continued to be focused on a) Enrollment at DHMC, University of Maryland, University of California and Brigham and Women's hospital, as well as completing patient follow up visits; (b) To identify the indicator for predicting unplanned reoperation and infection following high energy open fracture, based on analyzing imaging data and (c) Continually working on developing and validating the compact bone perfusion imaging system (cBPI) for bone perfusion in austere environments and/or forward operating units close to the battle field.

In the final quarter of the third year (12th quarter), our efforts remained concentrated on: (a) Enrollment at DHMC, UMDB, UCI, and BWH. In relation to enrollment, we successfully enrolled and imaged an additional 5 patients with open extremity fractures who underwent surgery at DHMC; (b) Completion of patient follow-up visits; (c) Analyzing the patient data collected thus far and identifying indicators that suggest patients may develop infections post-surgery; and (d) Validating our cBPI system through both phantom and small animal studies.

### *2) Specific objectives*

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.

### *3) Significant results or key outcomes*

To date 82 patients have been successfully imaged at DHMC, 15 at Shock Trauma, 0 at UCI, and 1 at 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. Furthermore, a compact bone perfusion imaging system (cBPI) for bone perfusion in austere environments and/or forward operating units close to the battle field, was developed and validated through phantoms and small animals.

*Nineth Quarter*

During 4-minute ICG imaging, blood often leaks or pools from the bone, forming streams or puddles on its surface. Due to the surface-perfusion-weighted nature of ICG imaging, these streams and puddles introduce imaging artifacts that influence bone perfusion assessment.

To mitigate these effects and enhance the accuracy of bone perfusion assessment, we have developed and optimized an image processing procedure based on a Top-hat filter. This procedure detects and excludes these blood stream and puddle areas from the bone perfusion evaluation. The kinetic curve showed significant alterations after artifact removal, specifically those caused by blood puddles. Additionally, the cross-sectional curve of maximum ICG intensity (Imax) was adjusted, rectifying the inaccurate trend. Instead of showing higher perfusion in severely injured areas than in minor ones, the corrected trend now reflects higher perfusion in areas with minor injuries compared to those with severe injuries.

When we categorized 48 patient cases into three groups based on the ratio of the area size with blood streams and puddles to the entire bone area within the surgical incision's field of view, the results were insightful. These groups had limited (24 cases), reasonable (16 cases), and high (8 cases) ratios. We found that in most cases where the ratio was less than 20%, these could be excluded from the perfusion analysis. By excluding areas with high artifact presence, we anticipate significant improvements in bone perfusion assessments.

During this quarter, we persistently worked on developing and validating the prototype imaging system. This system utilizes a gated signal to trigger the ICG excitation LED light source and the shutter of the cBPI, aiming

to eliminate ambient light interference from the surroundings. Our progress included: (1) Completed a light source subsystem with an array of 16 LEDs. Designing and developing a 3D-printed enclosure that compactly houses our camera and LEDs, ensuring effective heat dissipation, and (3) Fine-tuning the LED pulse and camera parameters to optimize stability, sensitivity, and spatial resolution. At a working distance of 30 cm, our field of view measures 12x22 cm, closely matching the commercialized system (SPY Elite). When compared to the SPY Elite system, which we previously used for bone perfusion imaging, our cBPI demonstrates superior sensitivity and dynamic range.

*Tenth Quarter*

We analyzed 26 patients who have completed 12-month follow up visits. Amongst these patients, 21 patients healed without complication, whereas 5 patients sustained a post-surgical infection. Bone perfusion-related parameters were calculated within the ROIs, after superficial blood artifact was removed. Based on the clinical outcomes, the patients have been divided into two groups of either non-infection or infection, and the parametric maps were analyzed by means of histograms and intensity thresholding in each of group. The results shown that area% with lower perfusion in infected group is higher than that in healed group. The maximum differences of area% was up to 18% when threshold intensity equaled 7.5. The area% difference of these two groups was gradually diminished when the threshold intensity increased to well-perfused regions. This result demonstrated that bone perfusion quantified using ICG-based DCE-FI during the orthopedic surgery has the potential to differentiate patients who will develop infection from those who will heal without complication.

When compared to the SPY PHI, the field of view for the cBPI is 51% of that of the SPY PHI. Additionally, the limit of detection (LoD) for the cBPI stands at 3 nM, which is marginally lower than that of the SPY PHI. The cBPI also boasts a lower noise floor than the SPY PHI in both high and low ambient environments. This suggests that our cBPI system offers better performance compared to the commercial imaging system (SPY PHI) that we have been using for bone perfusion..

*Eleventh Quarter*

During the 11th quarter, the Engineering team focused on identifying the indicator for predicting unplanned reoperation and infection following high energy open fracture. To identify the indicator for predicting unplanned reoperation and infection following high energy open fracture, we have preliminarily evaluated whether bone perfusion, reflected by DCE-FI, is related to the risk of recurrent infection within the 12 months after the initial surgery. 48 patients who have completed 12-month follow-up visits were included in this preliminary assessment. 24 patients did not experience a recurrent infection (Healed), whereas 15 patients sustained a recurrent infection within 3 months (Early infection), and 9 within 3 to 12 months (late infection). Based on the clinical outcomes, the patients have been divided into three groups of healed, early recurrent infection (within the first 3 months) and late recurrent infection (between 3 and 12 months), and Bone perfusion-related parameters were calculated within the bone area exposed in the surgical view. As the results, when we defined the ratio of the area with the bone blood flow below 15 (mL/min/100g) to the total bone area in the surgical insertion as the indicator, the mean value of this ratio in the early infection group is significantly different from that of late infection or healed group. Additionally, the mean value of the ratio in late infection group is only slightly higher than that of healed group. In addition, the ROC curve, which assesses the ability of the low bone blood perfusion area size to differentiate between 15 early infection cases and the remaining 33 cases of late infection and healed. The area under the curve (AUC) is calculated as 0.62, indicating a moderate level of accuracy in distinguishing between these groups. These findings suggests that a higher ratio of the low perfusion area, or the low perfusion area size can serve as the indicators for identifying cases at risk of recurrent infection within 3 months.

For improving the performance of, cBPI, we re-designed the system and made a new enclosure. The new configuration allows us to capture real-time fluorescence video and obtain white light images for motion correction purposes, compensating for mechanical motion of the imaging system as well as the subject's breathing. Additionally, we have successfully developed a battery sub-system to replace the large AC drive power supply used for the cameras and LEDs. This laptop-controllable battery sub-system enhances the portability and robustness of the entire imaging system, making it suitable for use in challenging environments such as austere environments or forward operating units near the battlefield.

*Twelfth Quarter*

For the technical development, we continually worked on preliminarily evaluating whether bone perfusion, as reflected by post-debridement DCE-FI, is associated with risk of complication in the 12 months after the surgery. 48 patients were included in this preliminary assessment. 47 patients have completed 12-month follow up visits and 1 patient developed infection before the end of follow up. Within these 48 patients, 41 patients healed without complication, whereas 7 patients sustained a post-surgical infection. Based on clinical outcomes, the patients have been divided into two groups of either non-infection or infection.

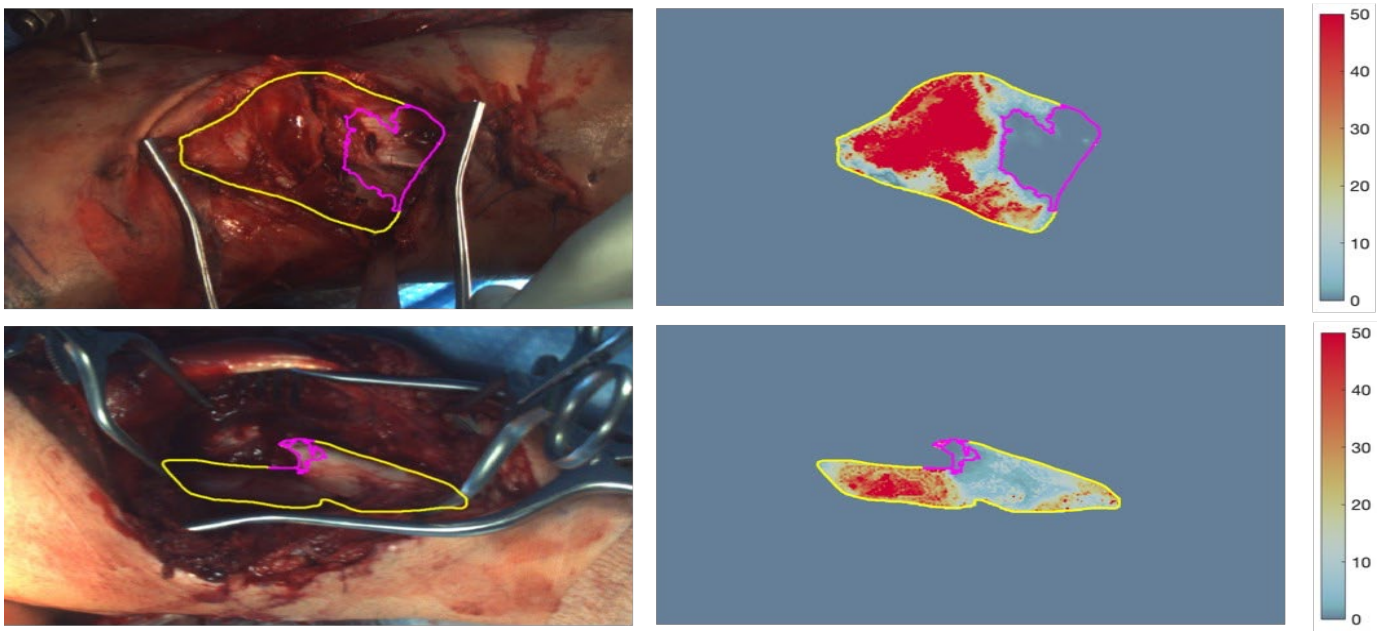



*Figure 1: Examples from two distinct cases. The top case (#12) developed an infection within 6 months, whereas the bottom case (#17) healed without any complications. In each set of images, the white-light photographs (on the left) and the blood flow intensity maps (on the right, with units in mL/min/100g) are displayed. Regions of interest (ROIs) are highlighted in yellow. Meanwhile, areas exhibiting low perfusion (with blood flow rates below 1 mL/min/100g) are encircled in magenta.*

Fig. 1 presents examples from two distinct cases. The top case (#12) developed an infection within 6 months, whereas the bottom case (#17) healed without any complications. In each set of images, the white-light photographs (on the left) and the blood flow intensity maps (on the right, with units in mL/min/100g) are displayed. Regions of interest (ROIs) are highlighted in yellow. Meanwhile, areas exhibiting low perfusion (with blood flow rates below 1 mL/min/100g) are encircled in magenta. It's evident from these images that the ratios of low perfusion areas for the infected and healed cases stand at 24.1% and 5.0%, respectively. Notably, cases that resulted in infection had post-debridement ROIs that displayed a larger proportion of poorly perfused bone areas compared to those that healed uneventfully.

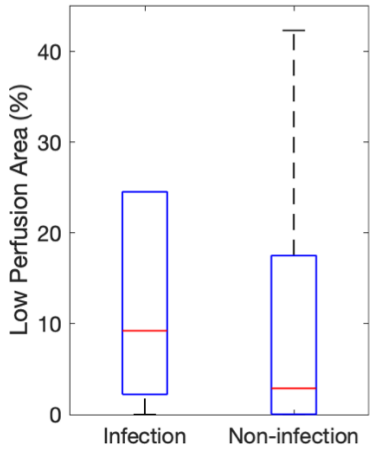
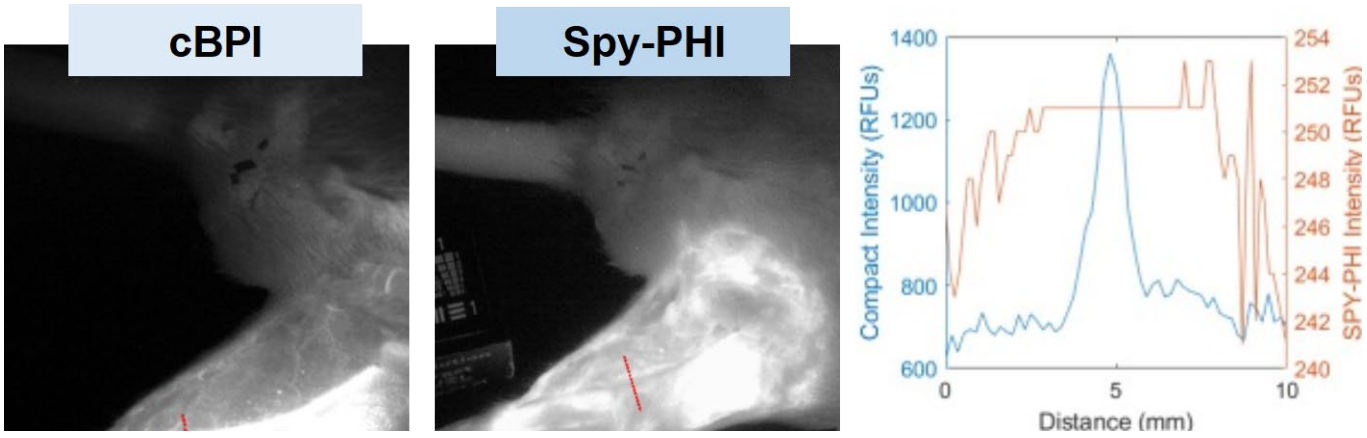



*Figure 2 boxplots representing the ratio of low perfusion areas, specifically under the blood flow threshold of 1 mL/min/100g, for both infected and healed groups.*

Fig. 2 depicts the boxplots representing the ratio of low perfusion areas, specifically under the blood flow threshold of 1 mL/min/100g, for both infected and healed groups. The most significant average ratio difference observed between the two groups was 12.4% for areas under this specific blood flow threshold. Furthermore, as the blood flow transitioned towards the well-perfused range, this ratio difference was seen to progressively decrease.

The results indicate that quantifying bone perfusion using ICG-based DCE-FI during orthopedic surgery can potentially distinguish between patients likely to develop infections and those who will recover without complications.

We conducted a study using small animals to compare the imaging performance of cBPI with the commercialized fluorescence imaging system, SPY-PHI. Four rats were involved in this experiment. On both day 1 and day 2, with their skin intact, each rat was imaged three times. We alternated between the cBPI and SPY-PHI imaging systems to counteract any residual effects of ICG. On the third day, the rats' skin was removed, and their bones were imaged both before and after inducing damage. Fig. 3 illustrates the rat imaging setup. The gray imaging device on the left is the SPY-PHI, while the enclosure colored in black and orange houses the camera and LED source for the cBPI. ICG was administered to the rats through a port implanted in their artery.



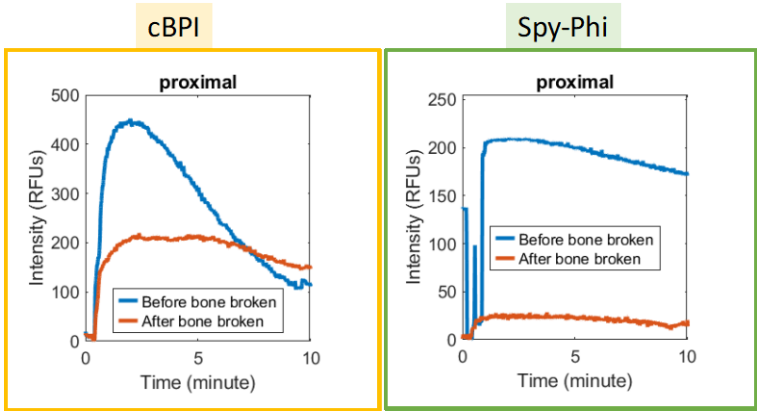




Fig.4 displays ICG images alongside the cross-sectional profiles of a blood vessel as captured by both the cBPI and SPY-PHI systems. The blue and red lines represent the vessel's cross-sectional profiles captured by the cBPI and SPY-PHI, respectively. The contrast between the blood vessel and the surrounding soft tissue in the image taken by the cBPI is considerably higher than that in the SPY-PHI image. This suggests that the spatial resolution of the cBPI is superior to that of the SPY-PHI. Furthermore, the flat segment of the blue profile indicates saturation of ICG intensity in the image captured by the SPY-PHI, highlighting its restricted dynamic range when compared to the cBPI. Fig. 5 showcases the kinetic curves of the proximal half of the bone both before and after damage. These curves confirm that the cBPI can effectively capture bone perfusion. In contrast, the SPY-PHI struggles to record bone perfusion prior to bone damage due to its limited dynamic range, which remains below 200 counts.

**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?**

*Describe briefly, what you plan to do during the next reporting period to accomplish the goals and objectives.*

In order to accomplish the goals of this project we will continue to image patients as well as collect follow up data on patients at DHMC, UMDB, and BWH. To date 82 patients have been successfully imaged at DHMC, 15 at Shock Trauma, 0 at UCI, and 1 at BWH.

In technical development, we will continually work on improving patient image process, towards the real time imaging display in the surgical room to guide orthopedic surgery, and identifying indicators that suggest patients may develop infections post-surgery. Based on the prototype cBPI system, we will focus on improving the sensitivity and stability of the system and validating it in the real patient imaging.

***4.*** **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

**What was the impact on the development of the principal discipline(s) of the project?**
*If there is nothing significant to report during this reporting period, state "Nothing to Report."*

*Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).*

We believe that bone perfusion/bone viability in the setting of severe trauma is an important indicator of post-surgical complications. Because of this, thorough debridement is the cornerstone of treatment for severe open fractures. However, in the absence of intraoperative methods to assess bone perfusion, extent of debridement is subjective and depends on surgeon's experience which may put patients under unnecessarily high risk for infection. As our results gained in year 3, indicated that area% with lower perfusion in infected group is higher than that in healed group. Thus, it is proofed that an indocyanine green (ICG)-based dynamic contrast-enhanced fluorescence imaging (DCE-FI) will able to provide surgeons with objective and quantitative data regarding bone perfusion.

Currently, most of the commercialized imaging systems operate on a continuous waveform (CW) light source and detection mechanism. However, to mitigate the effects of ambient light and decrease the size and weight of the LED power source in challenging environments, we incorporated time-gated technology into the imaging system. Our phantom and animal studies from year 3 indicate that cBPI can successfully execute DCE-FI with commendable sensitivity and stability. Moreover, the sensitivity and dynamic range of cBFI surpass those of the commercial imaging systems we currently use for bone perfusion, namely Spy Elite and SPY-PHI. Notably, this system relies on a computer-controlled battery for power. Its compact size combined with this feature makes it considerably more portable for use in forward operating units near battlefields, when compared to other commercial systems.

We expect that the outcomes of this research will elucidate the correlation between bone perfusion-based factors and critical clinical complications. This insight has the potential to revolutionize the treatment of severe open fractures. It offers surgeons a novel intraoperative tool, furnishing crucial data regarding healing potential and infection risk.

**What was the impact on other disciplines?**

*Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an 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?**

*Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:*

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report.

**What was the impact on society beyond science and technology?**

*Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:*

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report.

**5. CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

**Changes in approach and reasons for change**

*Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.*

Nothing to Report

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

*Describe problems or delays encountered during the reporting period and actions or plans to resolve them.*

Enrollment at all sites was continually delayed by the COVID-19 pandemic during the 2020-2021 years when all clinical research was halted due to pandemic restrictions. Over subsequent years, all institutions (UMB/STC, BWH, UCI and DHMC) have continued to face staffing-related challenges which has impacted patient enrollment. Furthermore, at all four institutions trauma activations are down as a result of the hospitals being full which has also impacted patient enrollment. At all institutions, PIs are continually working on staffing as well as to improve trauma transfer rates. At UMB and DHMC the orthopaedic surgery research infrastructure is 100% staffed. Trauma transfer rates have improved but remain not back to pre-COVID baselines.

BWH's Operating Rooms and research infrastructure continue to face staffing crises. Specifically and most importantly, these staffing shortages has made it impossible to complete the engineering adjustments needed to conform the data collected by the PHI device to the SPY Elite. Based off this, they have withdrawn from this study. We do not anticipate that this will impact study enrollment in a substantial way as they have only enrolled one patient thus far.

At DHMC, changes to the regulatory infrastructure has led to requested changes to how ICG is stored and administered. As a result of the change, there was a quality assurance issue around ICG dosing related to which patient weight was being used to calculate the weight-based dose. There were also changes to institutional requirements for ICG storage in collaboration with the Investigational Pharmacy. From August 3 to September 18 this study was placed on a voluntary hold while these regulatory changes were being implemented. The study is now off the voluntary hold and enrollment has resumed with several new enrollments for the month of September.

At UMB/STC the Spy Elite fluorescence imaging device broke, so they are currently on an enrollment hold as they work with Stryker to either fix or replace the imaging device. They anticipate resolution within 3-6 month time range and will resume patient enrollment as soon as possible.

Based on these challenges we are behind on enrollment. However, the study is active and we are continuing to enroll patients at the present.

**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**
  *Report only the major publication(s) resulting from the work under this award.*

  **Journal publications.** *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Elliott, J.T., Jiang, S., Henderson, E.R., Slobogean, G.P., O'Hara, N.N., Xu, C., Xin, J., Han, X., Christian M.L., Gitajn, I.L. (2022) Intraoperative assessment of bone viability through improved analysis and visualization of dynamic contrast-enhanced fluorescence imaging: technique report, OTA International, *e222*.

  **Books or other non-periodical, one-time publications.** *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to Report

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

  - Han, X., Bateman, L. M., Werth, P. M., Jiang, S., Gitajn, I. L., andElliott, J. T. (2023) Risk prediction on orthopaedic trauma patients for fracture-associated infection using dynamic contrast enhanced-fluorescence imaging In Proc SPIE Int Soc Opt Eng., Molecular-Guided Surgery: Molecules, Devices, and Applications IX, San Francisco, CA, USA 123610A
  - Elliott, J. T., Henderson, E., Streeter, S. S., Vemidov, a. D., Han, X., Tang, Y. *et al.* (2023) Fluorescence-guided and molecularly-guided debridement: identifying devitalized and infected tissue in orthopaedic trauma, In Proc SPIE Int Soc Opt Eng., Molecular-Guided Surgery: Molecules, Devices, and Applications IX, San Francisco, CA, USA 1236108
  - Henderson, E. R., Elliott, J. T., Jiang, S., Gitajn, I. L., Lee, J., Gibbs, S. *et al.* (2023) Proceduralist criteria for evaluating interface utility of novel imaging modalities in early phase clinical trials: evaluating the need for standardized criteria In Proc SPIE Int Soc Opt Eng., Molecular-Guided Surgery: Molecules, Devices, and Applications IX, San Francisco, CA, USA 123610F
  - Tang, Y., Gitajn, I. L., Cao, X., Han, X., Elliott, J. T., Yu, X., Bateman, L. M., Malskis, B. S., Fisher, L. A., Sin, J. M., Henderson, E. R., Pogue, B. W., and Jiang, S. (2023) Automated motion artifact correction for dynamic contrast-enhanced fluorescence imaging during open orthopedic surgery, In Proc SPIE Int Soc Opt Eng., Molecular-Guided Surgery: Molecules, Devices, and Applications IX, p 1236104, San Francisco, CA, USA.
  - Gitajn IL, Tang Y, Elliott JT, et al. Intraoperative real-time bone perfusion imaging, using ICG-based dynamic contrast-enhanced fluorescence imaging, has the potential to predict early infection recurrence. *OTA annual meeting*. 2023.
  - Gitajn IL, Tang Y, Elliott JT, et al. Bone perfusion quantified by intraoperative ICG-based dynamic contrast-enhanced fluorescence imaging has the potential to predict unplanned reoperation and infection after high energy open fracture. *OTA annual meeting* 2023.

- **Website(s) or other Internet site(s)**

Nothing to Report

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

| | | |
|---|---|---|
| Apr 2023 | 63/456,904 | Camera System and Method for Identifying Nonviable Tissue Using Fluorescent Tracer and Pulsed High-Intensity Fluorescent Excitation |

- **Other Products**

*Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:*

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to Report

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

**What individuals have worked on the project?**

*Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".*

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: Gerard Chang, MD
Project Role: Sub-Investigator (DHMC)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Devin Mullin
Project Role: Lead Research Coordinator-(DHMC)
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No change

Name: Holly Symonds
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:
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: Bethany Malskis
Project Role: Research Coordinator-(DHMC)
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No change, until she left institution on 09Jun2023

Name: Lillian Fisher
Project Role: Research Coordinator-(DHMC)
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No change

Name: Chelsey Recendez
Research Coordinator-(DHMC)
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: Chelsey has consented subjects, performed screening of subjects, completed case report forms and aided in obtaining subject imaging in the operating room.

Name: Jon Mikael Anderson
Project Role: Research Coordinator-(DHMC)
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No change

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: 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, until she left institution on 01Jul2023

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

Name: Heather Phipps
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Yasmin Degani
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Andrea Howe
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Haley Demyanovich
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Kathleen Healey
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Natasha McKibben
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Nicolas Zingas
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:

Nearest person month worked:
Contribution to Project: No change

Name: Casey Loudermilk
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Robert O'Toole, MD
Project Role: Professor / Surgeon (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Jason Nascone, MD
Project Role: Professor / Surgeon (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Marcus Sciadini, MD
Project Role: Professor / Surgeon (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Eric Hempen, MD
Project Role: Professor / Surgeon (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Marissa Bonyun, MD
Project Role: Professor / Surgeon (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: Marissa has ability to obtain informed consent, assess for inclusion criteria complete, complete imaging, review and sign off on CRF's

Mark Gage, MD
Project Role: Professor / Surgeon (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: Mark has ability to obtain informed consent, assess for inclusion criteria complete, complete imaging, review and sign off on CRF's

Name: Aaron Johnson, MD
Project Role: Professor / Surgeon (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: LaShann Selby
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Joshua Lawrence
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Kristin Turner
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Murali Kovvur
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: John Scolaro, MD
Project Role: Site Principal Investigator – University of California, Irvine
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: James Learned, MD
Project Role: Site Co-Investigator – University of California, Irvine
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Phillip Lim, MD
Project Role: Site Co- Investigator – University of California, Irvine
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Arya Amirhekmat
Project Role: Site Co- Investigator – University of California, Irvine
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Susan Demas
Project Role: Research Coordinator University of California, Irvine
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Michael Weaver
Project Role: Site Principal Investigator – Brigham and Women's Hospital
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Arvind Von Keudell, MD
Project Role: Co-Investigator – Brigham and Women's Hospital
Researcher Identifier:
Nearest person month worked:
Contribution to Project: No change

Name: Devon Brameier
Project Role: Research Coordinator Brigham and Women's Hospital
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No change

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

*If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.*

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:** ***N/A***

**QUAD CHARTS:**

See attached Quad Chart.

## 9. APPENDICES:

See attached copy of journal articles and Quad Chats.