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

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5e. TASK 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
None listed.

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TABLE OF CONTENTS

	Page
1. Introduction	5
2. Keywords	5
3. Accomplishments	5
4. Impact	10
5. Changes/Problems	11
6. Products	12
7. Participants & Other Collaborating Organizations	13
8. Special Reporting Requirements	17
9. Appendices	17

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?

1) Major activities

In the fifth quarter, our work was focused on (a) Enrollment at DHMC, University of Maryland Baltimore, University of California, and Brigham and Women's Hospital, which was continually delayed by the COVID-19 pandemic (b) Completing patient follow up visits (c) Continually working on developing imaging data process procedure to remove the motion effect due to the blood suction during the video taking period (d) Continuing to image eligible patients at DHMC, (e) Analysis the amputation patient data for understanding the changes of blood bone perfusion due to the different level of bone damage, and (f) Developing ICG based DCE-FI system for bone perfusion in austere environments and/or forward operating units close to the battle field. Virtual site visits were conducted with UMDB to review subject consent forms and subject data entered into the EDC so far at that time. A monitoring visit report was completed and sent to UMDB which noted various findings to be addressed appropriately.

In the sixth quarter, enrollment remained continually delayed by the COVID-19 pandemic, but seven additional patients with open extremity fractures who underwent surgery at DHMC were successfully enrolled and imaged in this study. Once enrollment had begun at University of California, Irvine (UCI) it was noted that

there was a significant recruitment barrier due to the high population of Spanish speaking patients. The informed consent form and HIPAA form for UCI were translated to Spanish and approved by DH-H IRB. The University of Maryland Baltimore (UMDB) had to temporarily pause enrollment due to significant staffing issues.

In the seventh quarter, our work continued to be focused on (a) Enrollment at DHMC, UMDB, UCI, and Brigham and Women's hospital (BWH) (b) Completing patient follow up visits; (c) Continuing to image eligible patients at DHMC and UMDB; (d) Continuing to work imaging data process procedure to eliminate in patient difference due to the arterial input function (AIF), (e) 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, and (f) Training new clinical research coordinators at DHMC and BWH's sites to ensure all study processes are followed correctly and remain consistent. Also, DHMC's Research Quality and Safety team worked with our team to ensure our regulatory binders contain all necessary documents. The Engineering team continued to develop and validate the prototype imaging system with a gated signal to trigger the ICG excitation LED light source and the shutter of the camera (cBPI) to eliminate the ambient light from the environment.

In the eighth quarter, our work continued to be focused on (a) Enrollment at DHMC, UMDB, UCI, and BWH (b) Completing patient follow up visits; (c) Continuing to image eligible patients at DHMC and UMDB (d) Continuing to work imaging data process procedure to eliminate in patient difference due to the arterial input function (AIF) and analysis the amputation patient data to understand the relationship between the bone damage level and perfusion parameters, and (e) Training new clinical research coordinators at DHMC and UMDB's sites to ensure all study processes are followed correctly and remain consistent. In regards to enrollment, eight additional patients with open extremity fractures who underwent surgery at DHMC were successfully enrolled and imaged in this study. UMDB's previous significant staffing issues improved and they enrolled two additional patients with open extremity fractures who underwent surgery at UMDB.
To date 55 patients have been imaged at DHMC, 8 at Shock Trauma, and 1 at BWH.
As for technical development, we continually worked on imaging data process procedure to eliminate in patient difference due to the AIF, analysis the amputation patients' image data, and improve the LED light source and pack up cBPI towards using it in the surgical room. We have improved the deconvolution process and optimized the pixel numbers for each deconvolution calculation.

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

Up to date, 55 patients have been imaged at DHMC, 8 at Shock Trauma, and 1 at BWH.

Fifth Quarter

In order to reduce motion artifacts on the ICG kinetic curves due to the surgeon occasionally suctions the blood leaking from the bone and surrounding tissues of the surgical incision, we have developed an imaging processing software code. After the motion correction, the range of the Dice indices over the imaging period has been reduced significantly, indicating the mismatching between the frames (due to the blood suction) has been reduced. In order to understanding the changes of blood bone perfusion due to the different level of bone damages, we have acquired ICG-based DCE-FI in patients (with/without feet) undergoing transtibial amputation. For each patient, three ICG-based DCE-FI sessions were obtained by SPY Elite system under the following conditions of severity in damage to bone blood flow: (1) baseline tibia; (2) after a transtibial osteotomy (simple fracture model – disrupting endosteal blood flow); and (3) after periosteal stripping (more complex higher energy fracture model – disrupting periosteal blood flow). DCE-FI images were processed and images representing maximum ICG intensity (Imax), ICG time-to-peak (TTP), and ICG ingress slope (IS; a metric of wash-in rate) were obtained. Six bone regions of interest (ROIs) were chosen with three proximal and three distal to the osteotomy. Bone perfusion parameters were calculated at each ROI in each clinical condition.

P-values < 0.05 indicated Imax and IS can differentiate the ROIs with the damage on only endosteal or endosteal + periosteal bone blood supply from the normal bone in both proximal and distal area, in patients with feet, (P-value (B-C) and P-value (B-S) while none of Imax nor IS can differentiate the damage on endosteal supply only from that on both periosteal and endosteal blood supply (P-value (C-S)). The statistical power is very limited on the cases with feet due to the limited sample size. A prototype imaging system (cBPI) was developed and started the validating process. This system is using a gated signal to trigger the ICG excitation LED light source and the shutter of the camera to eliminate the ambient light from the environment. Compared to a commercialized imaging system (SPY Elite, with room light off), the linearity of ICG intensity of this prototype cBPI system (with room light on) is significantly better than that of SPY Elite, however, the sensitivity of cBPI is 10 times lower than that of SPY Elite.

Sixth Quarter

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. 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) and are developing an image process procedure to deconvolute AIF from the imaged kinetics. Although the deconvolution process is still under development, we were able to see the peak values and the second peak reaching time of the ICG kinetics curves of an amputation patient were changed due to the AIF correction and the kinetics after AIF de-convolution is much closer to the expectation based on physiological knowledge. In this quoter, we have finished to develop the first version of camera control software for in house developed ICG based DCE-FI system This control software can be used to easily change the LED pulse and camera parameters to optimize the stability, sensitivity and spatial resolution, as well as further improve the user experience, of our imaging system. By using this control software and the first prototype cBPI, we have successfully imaged a rat fracture model.

Seventh Quarter

During the seventh quarter, the Engineering team continually worked on imaging data process procedure to eliminate in patient difference due to the AIF. Since the full deconvolute process is very time consuming and it is hard to be adapted into the surgical workflow for guiding the debridement real timely. We have worked on simplifying this process by investigated the AIF from all of the patients so far and tried to use a model with as less as possible variables to fit AIFs. Two models with each of 10 or 5 fitting parameters were developed and tested. As the results, the model has five variables has the less complexities while can fit the first in-flow part, which is the most important part for assessing bone perfusion nearly perfectly. We also tested whether we can use patient's clinical data to predicate AIF curves for those patients whose AIF measurement could not be gained during the ICG imaging. After testing many clinically relevant parameters, we found the patient weight is a factor which is most affect the AIF. We divided patients into the weight groups as #1<80 kg, #280-100 kg and #3>100kg and found the fitted values and time to peaks of the first peak in each of the weight groups are very close to the average AIFs, indicating our fitting can reflect measured AIF and possible to be used for the patients that could not gained AIF measurement during their intraoperative ICG imaging sessions. For cBFI development, we were working on optimum the LED pulse and camera parameters to optimize the stability, sensitivity and spatial resolution. Comparing to the commercial imaging systems that we are using for bone perfusion -Spy Elite, cBPI's power is lower but the dynamic range is larger. Since cBPI is using pulse detection technology, even the average power is lower, the peak power of the pulse which determine the signal to noise ratio of the ICG signal, can be several folders high than the average.

Eighth Quarter

For the technical development, we continually worked on imaging data process procedure to eliminate in patient difference due to the AIF, analysis the amputation patients' image data, and improve the LED light source and pack up cBPI towards using it in the surgical room. We have improved the deconvolution process and optimized the pixel numbers for each deconvolution calculation. After these improvements, the deconvolution time of each patient image with 4.5 minutes dynamic process can be reduced to several minutes.

Figure 1 shows maximum ICG (Imax) images before (Fig.1 (a)) and after (Fig.1 (b)) AIF deconvolution and AIF curves (Figure 1(c)) of the baseline imaging of two amputation patients. It can be seen clearly that the peak values and shapes of AIF are significantly different before and after AIF deconvolution eliminated the patient difference due to the effects of varying the ICG injection dose, injection rate, physiologic dispersion of dye and intravenous tubing volume propagate into the shape and magnitude of AIF during intraoperative fluorescence perfusion assessment. The much closed color in Imax images of two patients after AIF deconvolution indicated the feasibility of using DCE-FI to assess the bone perfusion and differentialize the damaged from normal bone since the inpatient difference of the normal bone (without damage) perfusion is small.

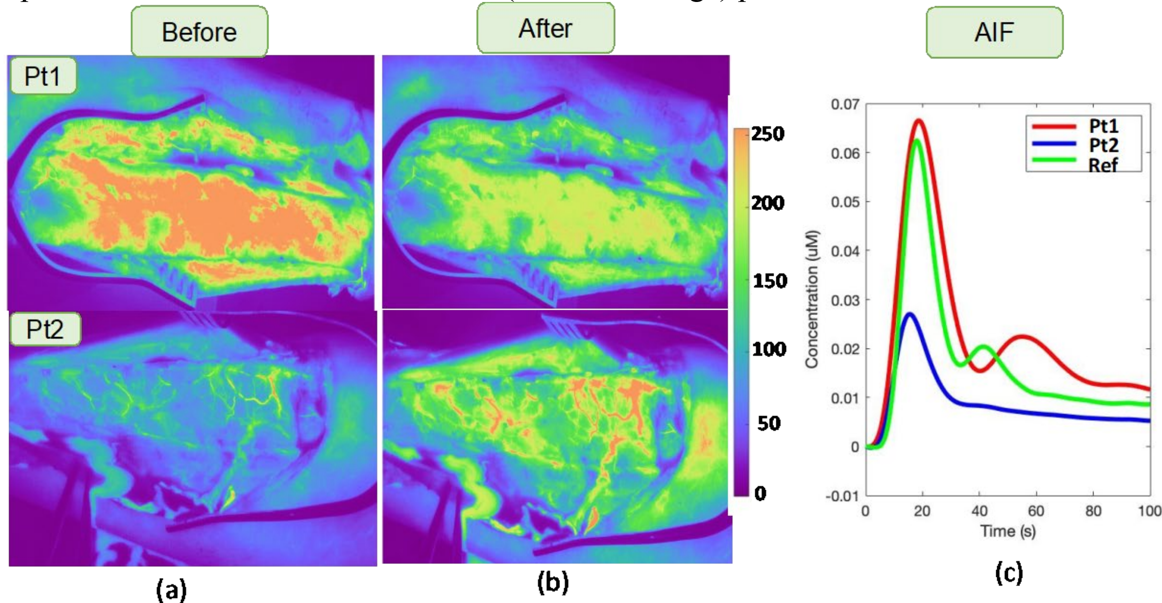

Figure 1 Maximum ICG images before (a) and after (b) AIF deconvolution and AIF curves (c), of the baseline imaging of two amputation patients.

For understanding whether DCE-FI can be used to establish the range and variation associated with bone/soft tissue perfusion in patients with an open fracture, and examine the relationship between perfusion and complications, fifteen adult patients (7 and 8 of foot on and off) undergoing below knee leg amputation has been imaged under three clinically relevant conditions. These three conditions were created at each patient limb, designed to mimic three levels of bone blood flow disruption after low-to-high energy fracture, and 0.1 mg/kg Indocyanine green (ICG) was intravenously injected in each condition: (1) baseline; (2) osteotomy (bone cut 15cm from the medial malleolus to disrupt endosteal blood flow, similar to a simple low energy fracture); (3) osteotomy and stripping (extensive soft tissue stripping proximal and distal to the osteotomy to disrupt both endosteal and periosteal blood flow, similar to a higher energy fracture). Figure 2 shows the boxplots of Imax in Group 1-Distal ROI, Foot-on (n=21), Group 2-Distal ROI, Foot-off (n=24), Group 3-Proximal ROI, Foot-on and Foot-off (n=45), at each condition of baseline (B), osteotomy (O), and Osteotomy+ Stripping (O+S), respectively. The p-values of <0.01 between each condition in all these three groups indicating DCE-FI can differentiate the damage level significantly.

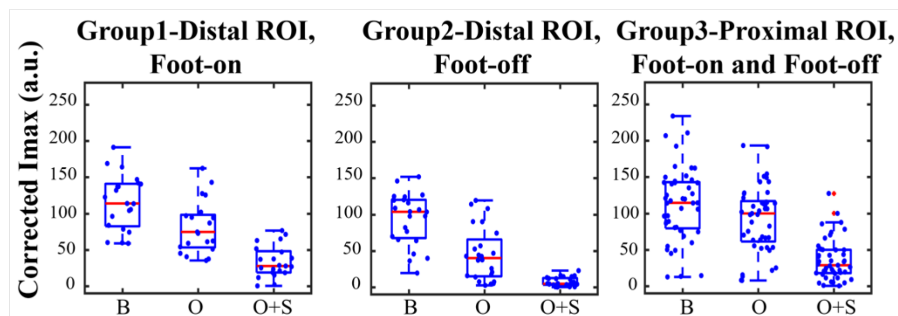

Figure 1 Boxplots represent the min, first quartile, median, third quartile, and max of Imax in three perfusion states. B: Baseline, O: Osteotomy, O+S: Osteotomy+ Stripping. Column

1-3: Group 1-Distal ROI, Foot-on (n=21), Group 2-Distal ROI, Foot-off (n=24), Group 3-Proximal ROI, Foot-on and Foot-off (n=45).

For increasing the light source power of cBPI, we redesigned drive circuits and packaging for LEDs. In addition, we tested all possible combinations of pulse timing, width, average power of the pulse and optimized all these parameters. After several iterations, the light source power increased 4 times with 16 LEDs.

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 image patients as well as collect follow up data on patients at DHMC, UMDB, and BWH. To date 55 patients have been imaged at DHMC, 8 at Shock Trauma, 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. 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::

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

Integrating AIF 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. 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.

So far, the commercialized imaging systems are based on continuous waveform (CW) light source and detection. For eliminating the ambient light effect and reduce the volume and weight of LED power source in austere environments, time gated technology has been utilized into the imaging system and achieved a imaging system with the features of very compacted in size, and easy to be carried into the forward operating units close to the battlefield. The animal study demonstrated cBPI is able to carry out DCE-FI with reasonable sensitivity and stability. By improving the LED light source power, optimizing the time gate parameters, and validating the system intraoperatively in the surgical room, we expect to gain the better or similar imaging performance as that of the commercialized systems.

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

Enrollment at all sites was continually delayed by the COVID-19 pandemic which also caused staffing issues at UMDB and UCI. UMDB has had several new staff members join their team and UCI is currently interviewing for another research coordinator to join their site.

To date, as a result of COVID-19 as well as unanticipated challenges with using a single central IRB (as opposed to each site using individual IRBs) we are still behind on patient enrollment.

Due to equipment availability and procurement, BWH's SPY Elite camera was replaced by the SPY PHI which is a comparable SPY device. However, engineering adjustments needed to be completed to conform the data collected by the PHI device to the SPY Elite, which caused a delay in data collection.

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**

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Journal publications.

Han, X., Demidov, V., Vaze, V. S., Jiang, S., Gitajn, I. L., and Elliott, J. T. (2022) Spatial and temporal patterns in dynamic-contrast enhanced intraoperative fluorescence imaging enable classification of bone perfusion in patients undergoing leg amputation, *Biomed Opt Express* 13, 3171-3186.

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, OTAI *in press*.

Books or other non-periodical, one-time publications.
Nothing to Report

Other publications, conference papers and presentations.

Tang, Y., et al. *Dynamic contrast-enhanced fluorescence imaging compared with MR imaging in evaluating bone perfusion during open orthopedic surgery*. In *SPIE Photonics West* 2022. San Francisco, CA.

Han, X., et al. *Intraoperative Indocyanine Green-based dynamic contrast-enhanced fluorescence imaging can effectively quantify bone perfusion*. in *63rd Annual Meeting, Society of Military Orthopaedic Surgeons*. 2021. Olympic Valley, CA.

Demidov, V., Clark, M. A., Bruza, P., Gitajn, I. L., and Elliott, J. T. (2022) Bone perfusion evaluation in high-energy fracture model of orthopaedic trauma with dynamic contrast-enhanced fluorescence imaging and optical coherence tomography, In *SPIE Photonics Europe*.

Elliott, J. T., I. (2022) Fluorescence-Guided Debridement in Orthopaedic Trauma: Challenges and Opportunities In *SPIE Photonics West*, San Francisco, **(Invited talk)**

Han, X., Demidov, V., Wirth, D., Byrd, B., Davis, S. C., Gitajn, I. L., and Elliott, J. T. (2022) Validation of dynamic contrast-enhanced bone blood flow imaging technique with fluorescent microspheres, In *SPIE Photonics West*, San Francisco.

Gitajn, I. L., Han, X., Cao, X., Christian, M., Chockbengboun, T., Henderson, E., and Jiang, S. (2022)
Quantify bone perfusion using Intraoperative ICG-based dynamic contrast-enhanced fluorescence imaging
In *Annual Meeting of Orthopaedic Trauma Association* Tampa, Florida.

- **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: Gerard Chang, MD
Project Role: Sub-Investigator (DHMC)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: Placing ICG study drug orders when Dr. Gitajn is away

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: Bethany has consented subjects, performed screening of subjects, completed case report forms and aided in obtaining subject imaging in the operating room.

Name: Lillian Fisher
Project Role: Research Coordinator-(DHMC)
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: Lillian 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: Jon Mikael assists with IRB modifications 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: 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: 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: LaShann has ability to consent subjects, perform screening of subjects, complete case report forms and aid in obtaining subject imaging in the operating room.

Name: Joshua Lawrence
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: Joshua has ability to consent subjects, perform screening of subjects, complete case report forms and aid in obtaining subject imaging in the operating room.

Name: Kristin Turner
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: Kristin has ability to consent subjects, perform screening of subjects, complete case report forms and aid in obtaining subject imaging in the operating room.

Name: Murali Kovvur
Project Role: Research Coordinator (R. Crowley)
Researcher Identifier:
Nearest person month worked:
Contribution to Project: Murali has ability to consent subjects, perform screening of subjects, complete case report forms and aid in obtaining subject imaging in the operating room.

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: Abigail Sagona
Project Role: Research Coordinator Brigham and Women's Hospital
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: No change, until she left institution on 01Jul2022

Name: Devon Brameier
Project Role: Research Coordinator Brigham and Women's Hospital
Researcher Identifier:
Nearest person month worked: 9
Contribution to Project: Devon has ability to consent subjects, perform screening of subjects, complete case report forms and aid in obtaining subject imaging in the operating room.

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

- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site)*

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS

QUAD CHARTS

9. APPENDICES

See attached copy of journal articles and Quad Chats.