

AWARD NUMBER: W81XWH-17-1-0287

TITLE: Multi-parametric Bioreactor for Functional Preservation of Vascularized Composite Allografts

PRINCIPAL INVESTIGATOR: Gerald Brandacher, MD

RECIPIENT: Johns Hopkins University

REPORT DATE: Oct 2019

TYPE OF REPORT: Annual Report

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

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14. ABSTRACT 1. More than half of the combat-related injuries per peer reviewed analyses of the Joint Theater Trauma Registry sustained by Warfighters in Iraq and Afghanistan involved extremities or craniofacial structures. An estimated 40% of all combat casualties in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) resulted in injuries to the extremities, face, and head and neck structures. Vascularized composite allotransplantation has increasingly become a viable clinical treatment option for the treatment of complex craniofacial and limb defects. To date, more than 100 patients worldwide have benefited from VCA, the majority receiving hand or face transplants. However, the transformational potential of VCA is severely limited by short preservation times (4 – 6 hours) 2. . This work will deliver ex vivo VCA perfusion technology intended to extend preservation time to 24 hours and minimize ischemia damage by efficient perfusion and multi-parametric monitoring.					
15. SUBJECT TERMS VCA preservation, electrical stimulation, biosensor					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON Gerald Brandacher, MD
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER (include area code)
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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Background. More than half of the combat-related injuries per peer reviewed analyses of the Joint Theater Trauma Registry sustained by Warfighters in Iraq and Afghanistan involved extremities or craniofacial structures. An estimated 40% of all combat casualties in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) resulted in injuries to the extremities, face, and head and neck structures. Vascularized composite allotransplantation has increasingly become a viable clinical treatment option for the treatment of complex craniofacial and limb defects. To date, more than 100 patients worldwide have benefited from VCA, the majority receiving hand or face transplants. However, the transformational potential of VCA is severely limited by short preservation times (4 – 6 hours) and all the logistical difficulties that come with this limitation. VCA survival is highly dependent on the ischemia injury happening during preservation. Consequently, organ preservation plays a major role in improving the clinical outcome of transplantation. Extracorporeal perfusion systems have demonstrated superior preservation outcome in different solid organs comparing to cold storage. Therefore there is critical need for developing preservation technology based on ex-vivo perfusion to enhance VCA preservation.

Objective/Hypothesis. This work will deliver ex vivo VCA perfusion technology intended to extend preservation time to 24 hours and minimize ischemia damage by efficient perfusion and multi-parametric monitoring.

Specific Aims.

Specific Aim 1. Engineer multi-parametric bioreactor system designed for preservation and real-time monitoring of NO/ROS in rat abdominal wall VCA. We designed stand-alone perfusion/electrical stimulation system maintaining viability of rat abdominal wall.

Specific Aim 2. Preserve viability and function of abdominal wall VCA up to 72 hours in bioreactor and establish the viability biomarker profile. We will develop ES protocol to enhance abdominal wall VCA preservation.

Specific Aim 3. Preserve whole extremity VCA in bioreactor and assess post-transplant viability and function. A new multi-parametric bioreactor will be designed based on the knowledge of bioreactor design we gain from the first aim and will preserve rat forelimb VCA for longer than 24 hours.

2. **KEYWORDS:** Provide a brief list of keywords (limit to 20 words).

Vascularized composite allograft, ex-vivo perfusion, biosensor, electrical stimulation, rat abdominal wall

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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.*

Specific Aim 1	Timeline	Progress
Major Task 1: Engineer multi-parametric bioreactor system designed for preservation and real-time monitoring of NO/ROS in rat abdominal wall VCA.	Months	
Task 1A: Design stand-alone perfusion/electrical stimulation system maintaining viability of rat abdominal wall	1-12	100%
Task 1B: Develop in-line sensors to measure concentrations of NO and ROS for non-invasive, real-time graft monitoring.	1-18	85%
Milestone(s) Achieved: ACURO approval for studies in Aims 2 & 3.		
Specific Aim 2		
Major Task 2: Preserve viability and function of abdominal wall VCA up to 72 hours in bioreactor and establish the viability biomarker profile.		
Task 2A: Optimize ES protocol to enhance abdominal wall VCA preservation.	6-18	60%
Task 2B: Preserve abdominal wall VCA for up to 72 hours through perfusion and ES. Utilize non-invasive measurements to establish a 'viability biomarker profile' and correlate with post-transplant viability.	6 – 24	65%
Milestone(s) Achieved:		
Specific Aim 3		
Major Task 3: Preserve whole extremity VCA in bioreactor and assess post-transplant viability and function.		
Task 3A: Re-design multi-parametric bioreactor to provide ES of the flexor and extensors forearm muscles of the rodent upper extremity transplant.	18 – 24	0%
Task 3B: Preserve rat forelimb VCA in bioreactor for 24 – 72 hours post-procurement. Assess ischemia-reperfusion injury, graft viability, and long-term function following bioreactor preservation.	18 - 36	0%
Milestone(s) Achieved:		

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.

Major activities:

- The overall housing system and perfusion loop with sensors.
- Minor characterization of the electrical stimulation system
- Preservation of rat abdominal wall VCA with colloid and electrolyte- supplemented perfusate
- Preservation of rat abdominal wall VCA with perfusate enriched with oxygen carriers; blood and hemoglobin
- Over the first year of the project a custom designed bioreactor and perfusion system had been built for studying VCA ex-vivo perfusion. There have been few modifications in the

oxygenator and valve setup in order to provide efficient oxygenation in the perfusion system. The high reproducibility in the results obtained from different experimental groups show that the abdominal wall model and the bioreactor is a robust system.

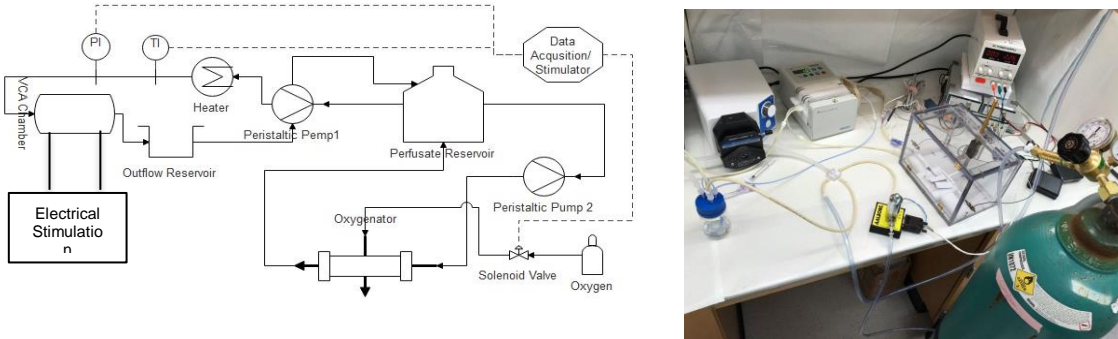


Figure 1. Perfusion system

Subtask 2.A: Optimize ES protocol to enhance abdominal wall VCA preservation.

The electrical stimulation system (ES) consists of a stimulation circuit and Arduino which delivers bi-phasic step signals within the range of desired frequency (10-50 Hz). To characterize the ES system, different electrodes made of platinum and carbon with different design have been tested. The commercially available self-adhesive carbon electrodes exhibit the most effective stimulation. The function of the electrodes during simultaneous perfusion has also been tested.

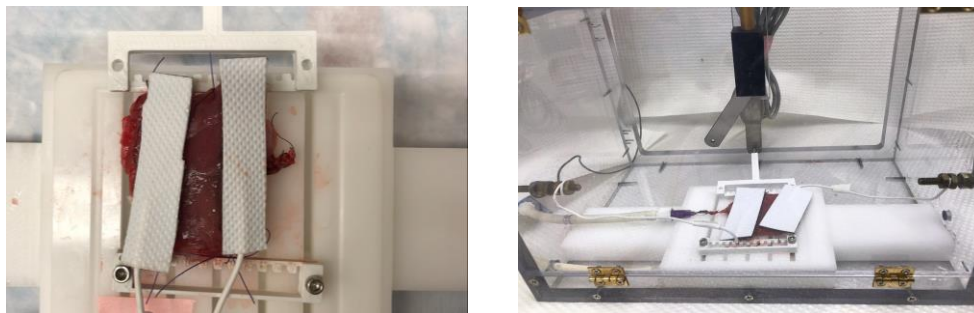


Figure 2 a. Self-adhesive electrode placed on the abdominal wall graft sutured to the clamps of the force sensor.

Subtask 2.B: Preserve abdominal wall VCA for up to 72 hours through perfusion and ES. Utilize non-invasive measurements to establish a ‘viability biomarker profile’ and correlate with post-transplant viability

Tissue swelling is the predominant issue with the ex-vivo perfusion systems. After 12 hours of perfusion with HTK there was detrimental tissue edema and changing the *perfusate composition* was investigated to lower the swelling.

- Increasing the oncotic pressure (osmotic pressure) has been pursued to decrease extravasation into the interstitial spaces. Albumin, a natural colloid, was the first option to

be studied with 25% as the optimum concentration. However, Dextran, a common colloid in the clinics, induced lower weight gain.

- Electrolyte concentration in the perfusate has also shown influence on the transport across the cells' membrane and consequently tissue swelling. Perfadex an extracellular solution with low potassium and high sodium and Dextran demonstrated the best outcome in lowering the tissue swelling due to ex-vivo perfusion (Figure 3).

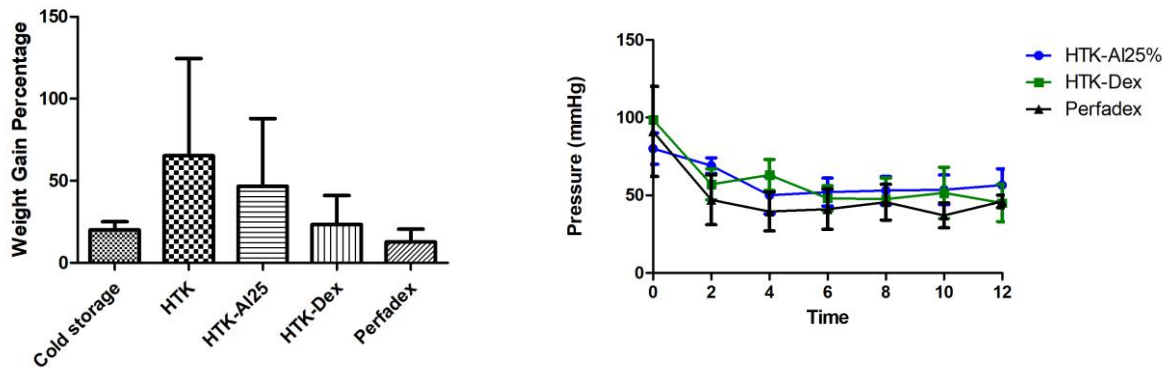


Figure 3. Weight gain percentage (after 12-hour perfusion) and perfusion pressure (at a constant flow rate of 0.3ml/min).

- Given this result shown in Figure 3, Perfadex was chosen as the base perfusate and we aimed at modifying it to resolve other issues such as low pH. THAM is the recommended buffer by the company for Perfadex but the optimum concentration for the ex-vivo perfusion of the VCA was unknown. We were able to find a concentration that maintain the pH within 7-7.3 during extended perfusion.
- The oxygen carrier is another essential component to preserve the graft. The hemoglobin-based oxygen carrier and red blood cells were chosen to be studied. The extracted hemoglobin from bovine red blood cells did not improve oxygen carrying capacity and its dissociation exacerbated damage in the muscle. The polymerized hemoglobin with high p50 is currently under investigation. At the same time a protocol for using red blood cell separated from blood was developed for 12 hour-perfusion.

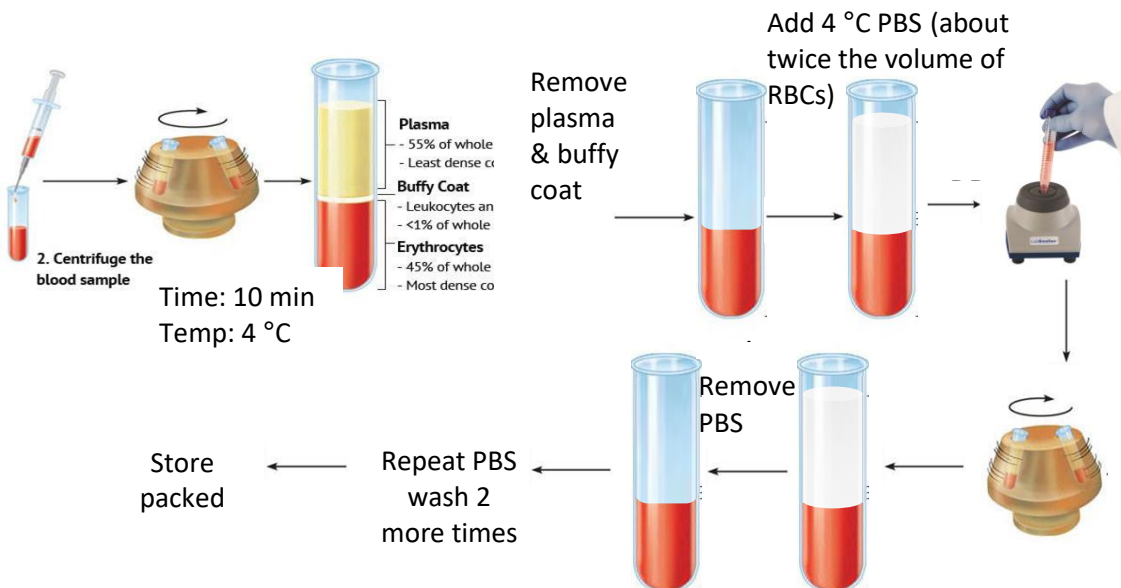


Figure 4 Red blood cell separation protocol from blood.

	Whole Blood	Bulk Perfadex Dilution		
	Initial	Initial	6 hr old	6 hr fresh
Hematocrit (%)	31.40	3.00	1.10	1.20
RBCs (M/uL)	6.13	0.47	0.22	0.20
Mean cell volume (fL)	51.20	63.80	50.00	60.00
Red cell distribution width- SD (fL)	37.70	35.00	35.90	54.80
Hemoglobin (g/dL)	11.30	0.80	0.40	0.30
Mean cell hemoglobin (pg)	18.40	17.00	18.20	15.00

Table 1 hematocrit in blood, after separation and dilution in the Perfadex and after perfusate replenishment at 6 hours of perfusion

- We have shown that 24 hours is the maximum time that cold storage is able to preserve the rat abdominal wall VCA successfully and enable survival post transplantation. Therefore, we extended perfusion to 24 hours with the exact condition of temperature, flow rate and perfusate as in previous studies. However the weight gain increased to 60%. We are currently working to modify the perfusate composition for 24 hours of perfusion.

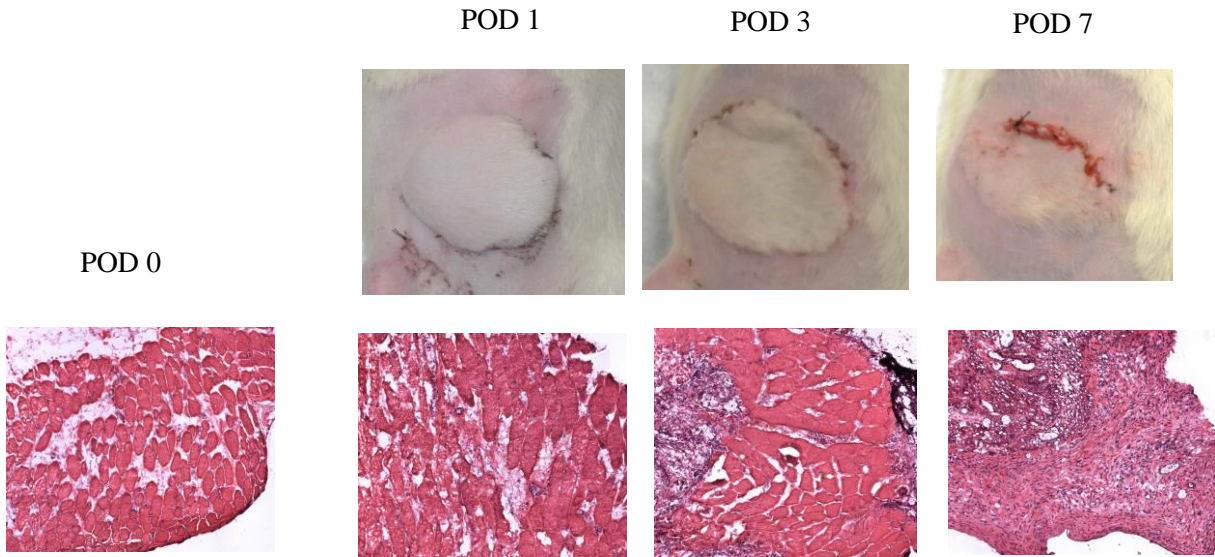


Figure 5 Transplantation of abdominal wall graft of 8-week Lewis rat preserved in Perfadex for 24 hours at 4C (POD0). Reperfusion damage has been demonstrated in the muscle biopsies at POD 3 and 7 but it did not result in graft rejection.

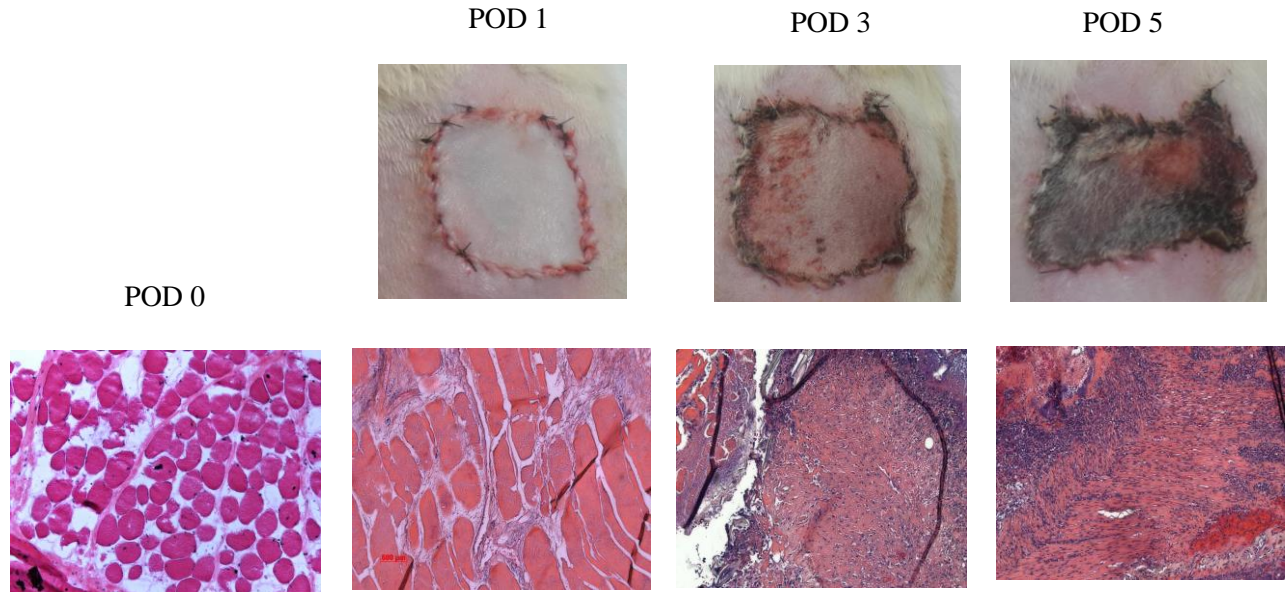


Figure 5 Transplantation of abdominal wall graft of 8-week Lewis rat preserved in Perfadex for 48 hours at 4C(POD0). Reperfusion damage and infiltration severely damaged the abdominal wall graft; graft showed necrosis on POD3 and the rat was euthanized on POD 5.

*Discussion of stated goals not met **These goals have been partially met due to delays in obtaining the IACUC and the subsequent ACURO approvals as well as due to delays in IRB approvals for the SVF isolation. However, we have since secured approvals for all of these elements and expect to achieve those goals over the next several months.***

There have been some other delays due to changes in plans discussed in more detail below in Section 5.

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

If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. “Training” activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. “Professional development” activities result in increased knowledge or skill in one’s area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Courses:

Individual Development Plans. Sara Salehi has 2 individual development meetings each year with Dr. Grayson (PI) to discuss the project as well as all other factors related to professional development.

Bi-weekly meetings: Dr. Grayson meets bi-weekly with Sara Salehi (PhD student), Carolyn Ton (MS student) and Renee Liu (undergraduate) to discuss detailed project plans.

Monthly meetings: Sara Salehi has had monthly meetings with Dr. Brandacher to discuss the project progress

Collaborative Meetings: The various labs meet several times a year to discuss overall project progress.

Papers:

Salehi, S., Tran, K., & Grayson, W. L. (2018). (Review Article): Advances in Perfusion Systems for Solid Organ Preservation. *The Yale Journal of Biology and Medicine*, 91(3), 301.

Conferences:

- Military Health System Research Symposium Poster presentation, “Evaluating the Impact of Perfusate Composition on the Viability of Abdominal Wall Allografts Following Ex Vivo Preservation”, August 2019
- American Society For Reconstructive Transplantation Biennial Meeting poster presentation, “Designing and Implementing A Multi-parametric Bioreactor For The Functional Preservation Of Vascularized Composite Allografts”. November, 2018.

How were the results disseminated to communities of interest?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

- Military Health System Research Symposium Poster presentation, “Evaluating the Impact of Perfusate Composition on the Viability of Abdominal Wall Allografts Following Ex Vivo Preservation”, August 2019
- American Society For Reconstructive Transplantation Biennial Meeting poster presentation, “Designing and Implementing A Multi-parametric Bioreactor For The Functional Preservation Of Vascularized Composite Allografts”. November, 2018.

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

If this is the final report, state "Nothing to Report."

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

- We will continue modifying the perfusate to minimize the ischemia and perfusion induced injury involving optimizing colloid concentration and adding antioxidant
- Investigate the optimum oxygen carrier (polymerized hemoglobin or separated red blood cells) and its oxygen delivery efficiency in collaboration with Dr. Andre Palmer's Lab at Ohio State University
- After confirming oxygen and nutrient delivery to the tissue we will optimize our electrical stimulation system to improve the graft preservation

4. **IMPACT:** Describe 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).

Nothing to Report.

What was the impact on other disciplines?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

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.

Nothing to Report.

What was the impact on technology transfer?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

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.*

The report of invention entitled “Controlled Ex-vivo Perfusion Associated with Electrical Stimulation System for Preservation of Vascularized Composite Allograft” has been submitted to Johns Hopkins office of technology transfer. JHU reference #D15952

What was the impact on society beyond science and technology?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

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 Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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.

- We have found that optimizing the perfusate composition is more challenging than initially anticipated. We tried using several clinically used preservation solutions, but these have to be modified via trial and error processes.
- We have had to establish new collaborations to obtain synthetic oxygen carriers to include in the perfusates.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report

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

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

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

5. **PRODUCTS:** List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state “Nothing to Report.”

- **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).*

Salehi, S., Tran, K., & Grayson, W. L. (2018). (Review Article): Advances in Perfusion Systems for Solid Organ Preservation. *The Yale Journal of Biology and Medicine*, 91(3), 301

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. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report

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

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to report

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

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report

- **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;*
- *biospecimen 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

6. 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.”

Example:

Name: Mary Smith
Project Role: Graduate Student
Researcher Identifier (e.g. ORCID ID): 1234567
Nearest person month worked: 5
Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.
Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award).

Name	Project Role	Researcher Identifier (e.g. ORCID ID):	Nearest person month worked	Contribution to project
Warren Grayson	Principal Investigator	0000-0001-6099-6469	3	Performed work towards bioreactor design. Worked on perfusion system process design.
Gerald Brandacher	Co-Investigator		1	Worked on animal model development
Gymama Slaughter	Co-Investigator		2	Worked on biosensor design
Sara Salehi	Graduate Student		12	Build perfusion system, establish abdominal wall perfusion and viability assessment
Byoung Chol Oh	Co-Investigator		.60	
Joseph Lopez	Co-Investigator		.60	
Samuel Fidder	Plastic Surgery Resident		6	Abdominal wall transplantation
Franka Messner	Plastic Surgery Resident		1	

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 there is nothing significant to report during this reporting period, state “Nothing to Report.”

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.

Active grants that have closed:
Title: Assessing the Effects of Wrapping Coaptation Site with Porcine Extracellular Performance Period: 04/01/2017 – 12/01/2018 Supporting Agency: AXOGEN CORPORATION Effort: .12 Calendar Months
Title: Phase II: Non-Toxic, Highly Effective Bioinspired Cryoprotectants Performance Period: 08/01/2018 – 06/29/2019 Supporting Agency: X-THERMA INC Effort:.12 Calendar Months
Title: Long term banking of Vascularized Composite Grafts using ice-free Performance Period: 01/01/2018 – 08/31/2019 Supporting Agency: TISSUE TESTING TECHNOLOGIES LLC Effort:.12 Calendar Months
Title: Translational Cell Based Immunomodulatory Therapies in Vascularized Composite Performance Period: 09/18/2013 – 09/17/2019 Supporting Agency: University of Pittsburgh/ DOD Effort:.60 Calendar Months
New active grants:
Title: Targeting Ischemia-Reperfusion Injury w/HO-1 Gene Therapy to Improve VCA Outcome Performance Period: 07/01/2018 – 06/30/2021 Supporting Agency: UCLA Effort: .12 Calendar Months
Title: A Novel Application of Normothermic Machine erfusion for Face Recovery Performance Period:09/01/2019 – 08/31/2022 Supporting Agency: USAMRAA Effort:.24 Calendar Months
Title: RT180041P2: Ethical factors impacting patients decsions to pursue VCA Performance Period: 09/30/2019 – 09/29/2022 Supporting Agency: USAMRAA Effort:1.20 Calendar Months

What other organizations were involved as partners?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:

Organization Name:

Location of Organization: (if foreign location list country)

Partner’s contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*
- *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); and*
- *Other.*

Nothing to Report.

7. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.

Nothing to Report.

QUAD CHARTS: If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.

8. **APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Nothing to Report.