

AWARD NUMBER: W81XWH-16-1-0758

TITLE: Complex Orbital Reconstruction

PRINCIPAL INVESTIGATOR: Warren Grayson, PhD

RECIPIENT: Johns Hopkins University

REPORT DATE: October 2020

TYPE OF REPORT: Annual Report

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

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13. SUPPLEMENTARY NOTES					
14. ABSTRACT 1. The number and severity of battlefield injuries to the craniofacial region increased significantly with the operations in Iraq and Afghanistan as has the survival of personnel with hemifacial injuries after ballistic trauma. Non-battlefield craniofacial injuries, including blunt trauma from motor vehicle accidents and falls, also provide a significant challenge in military operations and are relevant to the general population. Because of the complex nature of these injuries and the location in the craniofacial region, multiple tissue types suffer damage. These defects often involve a loss of maxillary and periorbital architecture resulting in poor malar projection, orbital dystopia, and visual sequelae. These craniofacial injuries often require numerous sequential complex surgeries that often do not achieve adequate aesthetic restoration or functional recovery. Therefore, there is a critical need for new solutions and improved surgical methods to treat these injuries. 2. This work will deliver GMP grade scaffolds comprised of human bone extracellular matrix (ECM) blended with polycaprolactone (PCL) into hybrid ECM-PCL scaffolds that can be 3D-printed into precise anatomical structures and effectively integrated with the patients' stromal vascular fraction cells for the treatment of geometrically complex bone defects in craniofacial trauma, focusing on the periorbital regions. This single distinct technology developed during Grant W81XWH-11-2-0022 will be integrated for this complex reconstruction of hard (bone) tissues in periorbital defects.					
15. SUBJECT TERMS Orbital reconstruction, bone graft, 3D-printing					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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1. **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Background. The number and severity of battlefield injuries to the craniofacial region increased significantly with the operations in Iraq and Afghanistan as has the survival of personnel with hemifacial injuries after ballistic trauma. Non-battlefield craniofacial injuries, including blunt trauma from motor vehicle accidents and falls, also provide a significant challenge in military operations and are relevant to the general population. Because of the complex nature of these injuries and the location in the craniofacial region, multiple tissue types suffer damage. These defects often involve a loss of maxillary and periorbital architecture resulting in poor malar projection, orbital dystopia, and visual sequelae. These craniofacial injuries often require numerous sequential complex surgeries that often do not achieve adequate aesthetic restoration or functional recovery. Therefore, there is a critical need for new solutions and improved surgical methods to treat these injuries.

Objective/Hypothesis. This work will deliver GMP grade scaffolds comprised of human bone extracellular matrix (ECM) blended with polycaprolactone (PCL) into **hybrid ECM-PCL scaffolds** that can be 3D-printed into precise anatomical structures and effectively integrated with the patients' stromal vascular fraction cells for the treatment of geometrically complex bone defects in craniofacial trauma, focusing on the periorbital regions. This single distinct technology developed during Grant W81XWH-11-2-0022 will be integrated for this complex reconstruction of hard (bone) tissues in periorbital defects.

Specific Aims. Based on the critical military need for surgical management of complex craniofacial injuries including the mid-face orbital region, and the emphasis on translational approaches the following specific aims will be addressed:

Specific Aim 1. Develop ECM-PCL composite biodegradable scaffolds for reconstructing periorbital, bony defects. We will develop protocols for printing scaffolds with the appropriate mechanical and degradation properties.

Specific Aim 2. Integrate 3D-printed ECM-PCL scaffolds for regenerating vascularized bone in cranial (mouse) and periorbital (pig) bone defects. The ECM-PCL scaffolds will be integrated with human SVF for mouse studies. For pig studies, we will 3D-print anatomically-shaped ECM-PCL scaffolds for the treatment of zygomatic bone segmental defects in Yorkshire pigs with and without porcine SVF.

Specific Aim 3. Transition steps for GMP production of clinical-grade ECM-PCL scaffolds will be performed.

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

Bone defects, periorbital, stem cells, reconstruction, trauma, porcine, craniofacial, scaffold

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: Develop defined bioactive, biodegradable ECM-PCL composite bone implants.		Months																
Task 1A: Define the formulation (wt/wt ratios) of ECM-PCL scaffolds.																		
a.	Evaluate quality of 3D prints as a function of ECM concentrations.	1-12	100%															
b.	Assess mechanics and degradation rates of ECM-PCL scaffolds with respect to ISO compliance.	1-12	100%															
Task 1B: Assess biological characteristics of 3D-printed ECM-PCL scaffolds.																		
a.	Perform proteomic analysis of bovine ECM pre- and post-printing.	1-24	100%															
b.	Cultivate human SVF in ECM-PCL scaffolds in vitro to assess osteoinductivity.	1-24	100%															
Milestone(s) Achieved: Task 1 will result in the optimized formulation of the ECM-PCL scaffolds based on bovine bone ECM to be 3D printed for use in the large animal periorbital defect.																		
Specific Aim 2																		
Major Task 2: Evaluation of scaffold technology for orbital bone reconstruction.																		
Task 2A: Calvarial bone defect reconstruction in murine model.																		
a.	Combine bioscaffolds with human SVF to regenerate vascularized bone in 4-mm calvarial defect in immunocompromised mice.	13-24	100%															
Task 2B: Periorbital bone defect reconstruction in porcine model.																		
a.	Short-term (6 weeks) and long-term (12 months) term assessments of zygomatic reconstruction in pig model.																	
<table border="1"> <thead> <tr> <th>Groups</th> <th>Defects per animal</th> <th>No. of animals</th> <th>Time-points</th> <th>Evaluation</th> </tr> </thead> <tbody> <tr> <td>Empty Defect</td> <td>2</td> <td>2</td> <td>12 months</td> <td>•Computed Tomography (Pre-op, post-op, 6 weeks, 12 months) •CBC/Chem</td> </tr> <tr> <td>Scaffold + Fibrin/SVF + PDGF</td> <td>2</td> <td>2</td> <td>6 weeks</td> <td>Pre-op, 6 weeks, 12 months •Tetracycline Administration Surgery •Calcein Administration 6 weeks</td> </tr> </tbody> </table>		Groups	Defects per animal	No. of animals	Time-points	Evaluation	Empty Defect	2	2	12 months	•Computed Tomography (Pre-op, post-op, 6 weeks, 12 months) •CBC/Chem	Scaffold + Fibrin/SVF + PDGF	2	2	6 weeks	Pre-op, 6 weeks, 12 months •Tetracycline Administration Surgery •Calcein Administration 6 weeks	10-36	90%
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Milestone(s) Achieved: Task 2 will demonstrate the utility of the scaffolds with and without autologous cells and with/without growth factor to regenerate vascularized bone in the periorbital regions. We will obtain valuable insight on materials design leading to more standardized, reproducible implants that can be manufactured for large, anatomical reconstructions with no problems in donor tissue acquisition.																		
Specific Aim 3																		
Major Task 3: Translation of technology for orbital bone reconstruction.																		
Task 3A: Transition to clinical grade manufacturing.																		
a.	Define SOPs for manufacturing scaffold.	13-24	80%															
b.	GMP production of anatomically shaped, ECM-PCL composite scaffolds.	13-36	10%															
Milestone(s) Achieved: Task 3 will establish the ground work for translation to a pre-clinical model and manufacture following GMP. Efficacy for composite tissue repair will be established along with translation.																		

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.

Here are the major accomplishments that were achieved during the period 31-Oct-2019 to 30-Oct-2020 in chronological order:

1. Developing a methodology to quantitatively assess post-operative bone growth
2. Harvesting of the porcine zygomas for biomechanical and histological analysis
3. Developing a platform to assess osseointegration of implants

1. Developing a methodology to assess post-operative bone growth

Table 1. CT Time points for different experimental groups. (Yellow shading indicates animals which were operated in December 2018 whereas green shading indicates the animals that were operated in June 2019).

Experimental Groups	No. of animals	CT Time Points	End of Study
Empty	2	Pre-Op, Post Op, 6wk, 12wk, 24wk, 52wk	52wk
Acellular	2		52wk
Cellular	4		52wk

Post-surgery, CT scans were performed on the pigs of different groups at the designated time points as shown in Table 1. The scans were analyzed using Materialise Mimics software. Briefly, the raw CT Dicom files were imported into mimics and thresholding was done at 226 HU (Hounsfield Units). The 3D skull volumes at different timepoints were registered with the corresponding volumes at PostOp timepoint and the VOI (volume of interest), in this case the implant, was isolated using the same wedge-shaped solid object (.stl file) which was used to create the segmental zygomatic defect initially as shown in figure 1. Once the VOI was isolated, a mask was created from it and the volume of the mask (i.e. the volume of the voxels contained in the respective mask) was recorded as **bone volume (BV)** for the respective time point. The total volume of the defect was calculated by performing a “wrap” function on the isolated VOI from the pre-op CT of the animals (performed a few weeks before the surgery) and was recorded as **total volume (TV)** for the



Figure 1. Isolation of VOI (volume of interest) i.e. the implant from the rest of the zygoma using the same wedge-shaped solid object (.stl) which was used for creation of the defect and respective implant design.

respective animal (constant for all time points).

Bone Volume/Total Volume (or BV/TV) was calculated and used a metric to compare bone regeneration across the different study groups. After 52 weeks, the quantitative CT evaluation demonstrated that there was negligible bone regeneration in the empty (control) group whereas the acellular and cellular groups exhibited significant neo bone formation. However, there was no statistically significant (2-way ANOVA) difference between the acellular and cellular groups.

2. Harvesting of the porcine zygomas for biomechanical and histological analysis

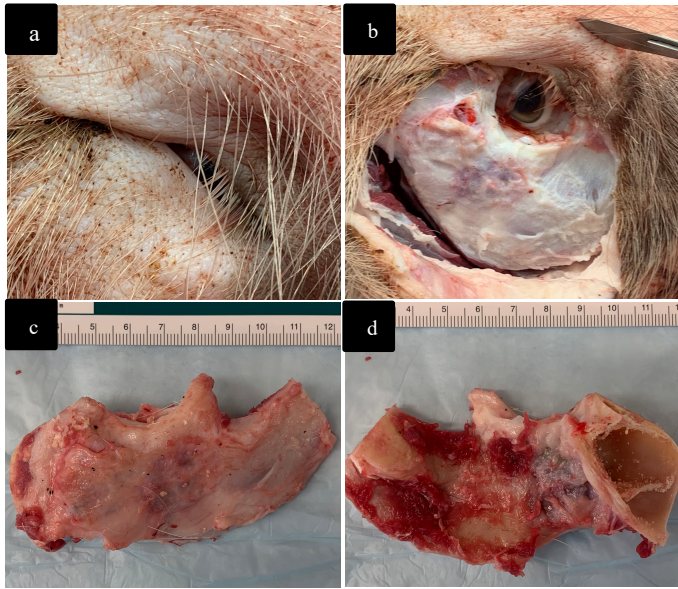


Figure 2. Harvesting of implants: (a) Gross overview of the peri-orbital region before implant harvest (b) removal of the skin exposing the zygoma (c) Lateral aspect of the harvested implant (d) Medial aspect of the harvested implant.

6 pigs (2 from acellular and 4 from cellular group) were sacrificed in the third week of June 2020 upon reaching their respective endpoints. Prior to euthanizing the pigs, 52-week timepoint CT scans of the skulls were acquired. The decapitated heads were shipped from Louisiana State University (on ice) where the animals were housed to Johns Hopkins University (JHU) where the zygomatic implants were harvested.

All the defects had healed really well with no signs of inflammation. There were no instances of abscess formation or swelling around the defect region during the course of the study (except for one of the zygomas where the anterior fixation tab of the scaffold had been displaced antero-laterally). There was adequate soft tissue coverage at the defect site and the defect boundaries were hardly identifiable (fig. 2). The zygomas of the pigs containing the scaffolds were harvested using a reciprocating saw. Upon

harvesting, five zygomas were immediately fixed in 10% formalin solution for histological analysis. The rest (n= 7) were wrapped in PBS saturated gauze and stored at -20°C for bio-mechanical testing in the future.

3. Developing a platform to assess osseointegration of implants

The harvested zygomas are anatomically complex and their inherent curvature makes it challenging to perform bio-mechanical test on a universal testing machine (UTM) platform. Herein, a testing platform for beam bending test of harvested porcine zygomas has been designed and its feasibility has been verified. Briefly, a sample specimen was potted into a mold using polymethyl methacrylate (PMMA) cement with the posterior aspect of the zygoma encased in the cement and the anterior aspect left as the free end (Fig. 3a). Once the cement solidified (in ~20 minutes), the mold acts as a gripping point of the specimen, for it to be secured into the UTM platform and thereafter, a descending beam applies load on the center of the scaffold (in a medial to lateral fashion) until it fractures at the scaffold-native bone interface (dotted yellow lines) proximal to the mold. A load v/s displacement curve could be analyzed which helps us to understand how the scaffold fails under load application (Fig. 3b). These profiles could then be used as a comparative metric to determine how well the scaffolds have integrated with the native bone.

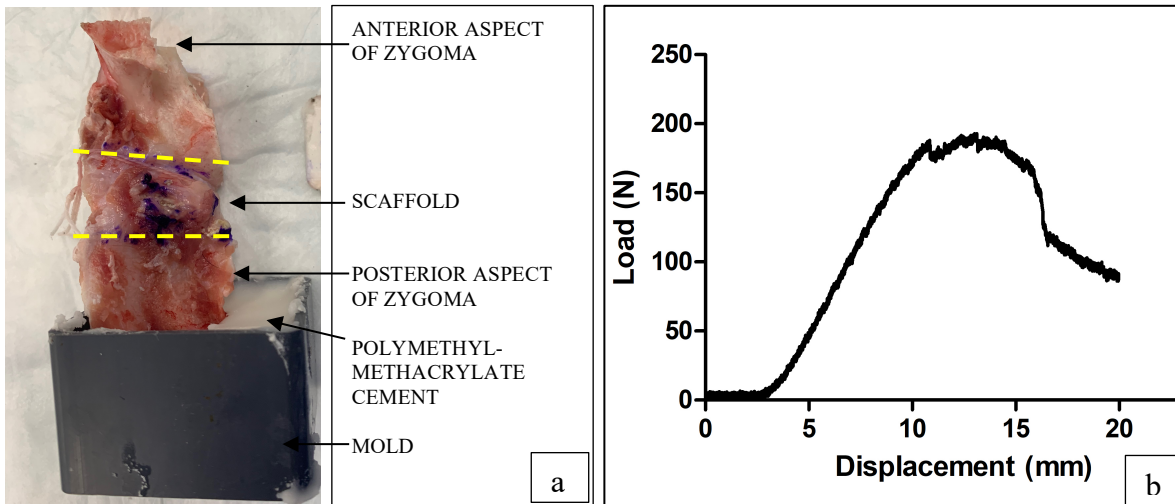


Figure 3. (a) Medial view of the harvested zygoma (containing the implant scaffold) potted in a mold using polymethyl methacrylate cement (dotted yellow lines indicate the scaffold-native bone interface) (b) Load v/s displacement curve for the beam bending test of the harvested zygoma.

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 in Section 5 below.

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.

One-on-one work with mentor: The PI has one-on-one meetings each year with Srujan Singh to discuss project related elements as well as all other factors related to professional development.

Weekly or bi-weekly meetings: Srujan Singh meets weekly in a group meeting with the PI, Dr. Warren Grayson where progress on the project is discussed.

Conferences: Abstract titled “Point-of-Care Cell-Based Strategy for Treating Large Craniofacial

Bone Defects” has been accepted for Oral presentation at the 11th World Biomaterials Congress 2020 and would be presented by Srujan Singh.

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.

Nothing to report.

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.

In the next reporting period we will be summarizing all the findings and quantitative results from the study namely – quantitative evaluation and comparison of new bone growth and osseointegration, microCT analysis demonstrating distribution of bone growth within the implants and histological analysis highlight inflammatory and local tissue response to the implants.

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).

Being able to demonstrate the capability to fabricate custom implants, isolate autologous SVF (stromal vascular fraction) and surgically secure the SVF loaded implants in the defects is a very crucial step towards developing a point-of-care bone tissue engineering strategy to treat clinically relevant large sized cranio-facial defects.

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.*

Full patent application in review:

US Patent Application: 15/739946

Grayson WL, Hung BP, Elisseeff JH, 3D-Printed Extracellular Matrix Mixture and ECM Scaffolds Made with Polycaprolactone and decellularized bone.

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.

Nothing to Report

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

6. **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).*

Nothing to report.

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.*

1. Poster presentation at TERMIS-Americas: **E. L. Nyberg**, A. Farris, W. Grayson. *Assessing the Osteogenic Potential of Adipose-derived Stromal Vascular Fraction Cells*. Poster at the Tissue Engineering and Regenerative Medicine International Society Annual Conference. Charlotte, North Carolina. (2017) **** Winner, Student and Young Investigator Section ****
2. Poster presentation at JHU Department of Medicine Annual Retreat **E. L. Nyberg**, A. Farris, W. Grayson. *Assessing the Osteogenic Potential of Adipose-derived Stromal Vascular Fraction Cells*. (2018) **** Finalist, School of Engineering Trainee ****
3. Invited presentation at World Congress of Biomechanics. "Design and Manufacture of 3D-Printed Scaffolds for Regeneration of Massive Craniofacial Bone Loss", Ethan Nyberg, Aine O'Sullivan, Warren Grayson.
4. Oral presentation at the Northeast Bioengineering Conference "3D-Printing Heterogeneous Porous Patterns in Tissue Engineered Bone Scaffolds", Aine O'Sullivan, Ethan Nyberg, and Warren Grayson.

- **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.

Full patent application in review:
US Patent Application: 15/739946
Grayson WL, Hung BP, Elisseeff JH, 3D-Printed Extracellular Matrix Mixture and ECM Scaffolds Made with Polycaprolactone and decellularized bone.

• **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

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.”

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	12	Oversaw animal studies
Srujan Singh	Graduate Student		12	Print Quality Assessment CT Scan Analysis
Yuxiao Zhou	Post Graduate Candidate		2	CT Analysis
Emma Whitehead	Undergraduate Student		10	CT Analysis and Registration

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:

NSF CAREER Award - 1350554

Role: PI

Period: 05/15/14 – 05/14/19 0.6 CM

Program Officer: Steven Peretti, speretti@nsf.gov

Title: Modeling Stem Cell Decision Making During Vascularized Bone Development

Maryland Stem Cell Research Fund – Investigator-Initiated Research Proposal

Role: PI

Period: 07/01/16 – 06/30/19 1.2 CM

Program Officer: Dan Gincel, dgincel@tedco.md

Title: Engineering Contractile Muscle for Treatment of Volumetric Muscle Loss

New active grants:

Congressionally Directed Medical Research Programs

Role: Multi-PI (Contact PI)

Period: 9/30/17-9/29/20 1.2 CM

Scientific Officer: Nicole Enman nicole.m.enban.ctr@mail.mil

Title: Multi-Parametric Bioreactor for Functional Preservation of Vascularized Composite Allografts

Maryland Stem Cell Research Fund

Role: PI

Period: 07/01/18 – 02/29/20 0.6 CM

Program Officer: Dan Gincel, dgincel@tedco.md

Title: 3D-Printed, Oxygen-Delivering Scaffolds for Regenerating Vascularized Craniofacial Bone

R01 – National Institute of Dental and Craniofacial Research

Role: Contact PI (Grayson/Pathak)

Period: 04/01/19 – 03/31/24

Program Officer: Nadya Lumelsky nadyal@nidcr.nih.gov

Title: Oxygen-Eluting Scaffolds for Cranial Bone Regeneration

Maryland Stem Cell Research Fund – Discovery Award

Role: Co-I

Period: 07/01/19 – 06/30/21

Program Officer: Dan Gincel, dgincel@tedco.md

Title: An engineered orthogonal growth factor for targeted stimulation of bone repair

R01 – National Institute of Arthritis, Musculoskeletal and Skin Disorders

Role: Contact PI (Grayson/Lee)

Period: 07/01/20 – 06/30/25

Program Officer: Aron Marquitz

Title: Regenerating Vascularized and Innervated Skeletal Muscle to Treat VML Defects

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.*

Geistlich Pharma North America Inc.

202 Carnegie Center

Princeton, NJ 08540

Provided in-kind support by contributing Bio-Oss, the clinical grade bone ingredient in the implants.

8. 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.

9. **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.