# Final Progress Report for Research Projects Funded by Health Research Grants

Instructions: Please complete all of the items as instructed. Do not delete instructions. Do not leave any items blank; responses must be provided for all items. If your response to an item is "None", please specify "None" as your response. "Not applicable" is not an acceptable response for any of the items. There is no limit to the length of your response to any question. Responses should be single-spaced, no smaller than 12-point type. The report **must be completed using MS Word**. Submitted reports must be Word documents; they should not be converted to pdf format. Questions? Contact Health Research Program staff at 717-783-2548.

1. **Grantee Institution:** The Pennsylvania State University

2. **Reporting Period (start and end date of grant award period):** 1/1/2010 - 12/31/2013

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** John Anthony, MPA

4. **Grant Contact Person's Telephone Number:** 814 935 1081

5. **Grant SAP Number:** 4100050904

6. **Project Number and Title of Research Project:** 21: Biomechanical Failure and Loosening Characteristics of a Novel Posteriorly Augmented Glenoid Component

7. **Start and End Date of Research Project:** 9/1/2010 to 9/30/2011

8. **Name of Principal Investigator for the Research Project:** April D. Armstrong, MD

9. **Research Project Expenses**.

   9(A) Please provide the amount of health research grant funds spent on this project for the entire duration of the grant, including any interest earned that was spent:

   $ 38,050.03: 24,758.83 (direct) + 13,291.20 (indirect)

   9(B) Provide the last names (include first initial if multiple individuals with the same last name are listed) of **all** persons who worked on this research project and were supported with health research funds. Include position titles (Principal Investigator, Graduate Assistant, Post-doctoral Fellow, etc.), percent of effort on project and total health research funds expended for the position. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

| Last Name | Position Title | % of Effort on Project | Cost |
|---|---|---|---|
| None | | | |

9(C) Provide the names of **all** persons who worked on this research project, but who *were not* supported with health research funds. Include position titles (Research Assistant, Administrative Assistant, etc.) and percent of effort on project. For multiple year projects, if percent of effort varied from year to year, report in the % of Effort column the effort by year 1, 2, 3, etc. of the project (x% Yr 1; z% Yr 2-3).

| Last Name | Position Title | % of Effort on Project |
|---|---|---|
| Armstrong | Associate Professor | 2% |
| Lewis | Instructor | 2% |
| Sathyendra | Resident | 1% |
| Paul | Research Associate | 2% |
| Brenza | Student | 1% |

9(D) Provide a list of **all** scientific equipment purchased as part of this research grant, a short description of the value (benefit) derived by the institution from this equipment, and the cost of the equipment.

| Type of Scientific Equipment | Value Derived | Cost |
|---|---|---|
| None | | |

**10. Co-funding of Research Project during Health Research Grant Award Period.** Did this research project receive funding from any other source during the project period when it was supported by the health research grant?

Yes_____ No_____X____

If yes, please indicate the source and amount of other funds:

**11. Leveraging of Additional Funds**

11(A) As a result of the health research funds provided for this research project, were you able to apply for and/or obtain funding from other sources to continue or expand the research?

Yes___X_____ No_____

If yes, please list the applications submitted (column A), the funding agency (National Institutes of Health—NIH, or other source in column B), the month and year when the application was submitted (column C), and the amount of funds requested (column D). If

you have received a notice that the grant will be funded, please indicate the amount of funds to be awarded (column E). If the grant was not funded, insert "not funded" in column E.

Do not include funding from your own institution or from CURE (tobacco settlement funds). Do not include grants submitted prior to the start date of the grant as shown in Question 2. If you list grants submitted within 1-6 months of the start date of this grant, add a statement below the table indicating how the data/results from this project were used to secure that grant.

| A. Title of research project on grant application | B. Funding agency (check those that apply) | C. Month and Year Submitted | D. Amount of funds requested: | E. Amount of funds to be awarded: |
|---|---|---|---|---|
| Strain and fatigue mechanics in bone surrounding cemented orthopaedic implants | X NIH<br>☐ Other federal (specify:_____)<br>☐ Nonfederal source (specify:_) | October 2011 | $ 229,500.00 | scored but not yet funded |

11(B) Are you planning to apply for additional funding in the future to continue or expand the research?

Yes____X____ No_____

If yes, please describe your plans:

In addition to the above grant application that we submitted to the NIH, we plan to submit for funding from the Orthopaedic Research and Education Foundation and from orthopaedic implant companies such as Zimmer.

**12. Future of Research Project.** What are the future plans for this research project?

Our overall hypothesis is that a posteriorly augmented glenoid component and implantation method can be developed that reduces rates of loosening and other clinical complications. Our general approach is to develop novel, validated micro-computed tomography (micro-CT) and computational approaches for comprehensively assessing mechanics of implanted constructs. This research will advance the general understanding of glenoid loosening mechanics, and is potentially generalizable to other orthopaedic implants.

Specifically, we aim to perform the following: (1) Determine and compare trabecular bone strains in native and implanted cadaveric glenoids using micro-CT-based strain mapping; (2) Subject implanted specimens to cyclic, physiologic glenohumeral loads and characterize damage evolution using micro-CT; (3) Predict strain distributions using computational micro-finite element models and then compare to the above experimental results.

13. **New Investigator Training and Development**. Did students participate in project supported internships or graduate or post-graduate training for at least one semester or one summer?

Yes___X_____ No_____

If yes, how many students? Please specify in the tables below:

| | Undergraduate | Masters | Pre-doc | Post-doc |
|---|---|---|---|---|
| Male | 1 | | | |
| Female | | | | |
| Unknown | | | | |
| **Total** | **1** | | | |

| | Undergraduate | Masters | Pre-doc | Post-doc |
|---|---|---|---|---|
| Hispanic | | | | |
| Non-Hispanic | 1 | | | |
| Unknown | | | | |
| **Total** | **1** | | | |

| | Undergraduate | Masters | Pre-doc | Post-doc |
|---|---|---|---|---|
| White | 1 | | | |
| Black | | | | |
| Asian | | | | |
| Other | | | | |
| Unknown | | | | |
| **Total** | **1** | | | |

14. **Recruitment of Out-of–State Researchers**. Did you bring researchers into Pennsylvania to carry out this research project?

Yes_____ No_____X____

If yes, please list the name and degree of each researcher and his/her previous affiliation:

15. **Impact on Research Capacity and Quality**. Did the health research project enhance the quality and/or capacity of research at your institution?

Yes____X____ No_____

If yes, describe how improvements in infrastructure, the addition of new investigators, and other resources have led to more and better research.

We developed new capability in our biomechanics laboratory for controlled cyclic

mechanical loading and high-resolution optical and radiographic imaging of specimens. We expect these capabilities will be utilized in future projects within the overall College of Medicine. (In addition to intradepartmental research, our lab capabilities are often used for collaborative projects with researchers from departments such as Plastic Surgery and Anatomy.)

Additionally, we obtained and gained expertise using a powerful software program (Avizo, VSG US, Burlington MA) for visualization and analysis of 3D medical images. We have begun to apply this software to additional research projects within the Department of Orthopaedics, resulting in improved capability and research quality in these other projects.

**16. Collaboration, business and community involvement.**

16(A) Did the health research funds lead to collaboration with research partners outside of your institution (e.g., entire university, entire hospital system)?

Yes____X____ No____ _____

If yes, please describe the collaborations:

We had discussions with engineers and other representatives from the implant company Zimmer regarding our testing protocol and overall aims of the research.

16(B) Did the research project result in commercial development of any research products?

Yes_____ No___X_____

If yes, please describe commercial development activities that resulted from the research project:

We investigated patenting possibilities for the posterior step glenoid implant but with the help of the intellectual property department this was determined not feasible

16(C) Did the research lead to new involvement with the community?

Yes_____ No____X_____

If yes, please describe involvement with community groups that resulted from the research project:

**17. Progress in Achieving Research Goals, Objectives and Aims.**

List the project goals, objectives and specific aims (as contained in the grant application's

strategic plan). Summarize the progress made in achieving these goals, objectives and aims for the entire grant award period. Indicate whether or not each goal/objective/aim was achieved; if something was not achieved, note the reasons why. Describe the methods used. If changes were made to the research goals/objectives/aims, methods, design or timeline since the original grant application was submitted, please describe the changes. Provide detailed results of the project. Include evidence of the data that was generated and analyzed, and provide tables, graphs, and figures of the data. List published abstracts, poster presentations and scientific meeting presentations at the end of the summary of progress; peer-reviewed publications should be listed under item 20.

This response should be a DETAILED report of the methods and findings. It is not sufficient to state that the work was completed. Insufficient information may result in an unfavorable performance review, which may jeopardize future funding. If research findings are pending publication you must still include enough detail for the expert peer reviewers to evaluate the progress during the course of the project.

Health research grants funded under the Tobacco Settlement Act will be evaluated via a performance review by an expert panel of researchers and clinicians who will assess project work using this Final Progress Report, all project Annual Reports and the project's strategic plan. After the final performance review of each project is complete, approximately 12-16 months after the end of the grant, this Final Progress Report, as well as the Final Performance Review Report containing the comments of the expert review panel, and the grantee's written response to the Final Performance Review Report, will be posted on the CURE Web site.

**There is no limit to the length of your response. Responses must be single-spaced below, no smaller than 12-point type. If you cut and paste text from a publication, be sure symbols print properly, e.g., the Greek symbol for alpha (α) and beta (ß) should not print as boxes (□) and include the appropriate citation(s). DO NOT DELETE THESE INSTRUCTIONS.**

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*A. Planned project goals, objectives and specific aims (as contained in the grant application's strategic plan):*

*Biomechanical Failure and Loosening Characteristics of a Novel Posteriorly Augmented Glenoid Component* – The objective of this study is to characterize the mechanics of novel and standard cemented Total Shoulder Arthroplasty glenoid implants subject to cyclic mechanical loading. We have developed a novel glenoid implant that includes a posterior augmentation to compensate for posterior bone loss often found in shoulder osteoarthritis. We seek to understand the loosening resistance and micro-mechanics of the bone-cement-implant interface in both this implant and standard glenoid implants. Micro-computed tomography will be used to image the implant fixation after various stages of controlled cyclic loading applied to simulate physiologic shoulder activity.

Loosening of the artificial glenoid implant is the most common complication following total shoulder arthroplasty. Glenoid component implantation is often difficult due to posterior glenoid bone loss associated with osteoarthritis. A novel posteriorly augmented step glenoid implant which compensates for bone loss has been developed in our laboratory. The objective of this study is to biomechanically characterize the loosening performance of this novel implant subject to cyclic loading, as compared to a standard glenoid implant. In addition we expect to advance the general understanding of the loosening mechanics of the glenoid, and potentially other cemented orthopaedic implants, through novel analysis of high resolution X-ray microcomputed tomography (micro-CT) scans obtained at various stages of the fatigue process.

Specific Aim 1: Quantify number of cycles until initiation of fixation fracture for a novel posterior step glenoid implant and a standard three-pegged glenoid implant. An ASTM standard method for cyclically loading glenoid implants implanted in bone substitute will be modified to include an anterior-posterior directed mechanical load. We will perform novel micro-CT analysis of the bone-cement-interface at every 10,000 loading cycles until fracture initiation, and then at 70,000 cycles. Our hypothesis predicts an equivalent or greater number of cycles before initiation of a 5 mm fixation fracture crack for the posterior step glenoid compared to the standard implant.

Specific Aim 2: Quantify toggle displacement of the anterior and posterior glenoid articular rims for the posterior step glenoid implant and the standard implant. Using the cyclic loading protocol described above, implant toggle displacement will be measured before cycling, at fracture initiation, and after 70,000 loading cycles. Our hypothesis predicts equivalent or less toggle displacement for the posterior step glenoid compared to the standard implant.

Specific Aim 3: Repeat testing with the same loading protocol but with implanting the glenoid prostheses in a small number of cadaveric scapular bone specimens instead of the bone substitutes. We expect that the findings obtained in Specific Aims 1 and 2 will be supported.

*B. Summary of progress made in achieving these goals, objectives and aims:*

We have made substantial progress in characterizing the micromechanics of novel and standard cemented glenoid implanted specimens under cyclic fatigue loading. We have successfully implanted several different components into human cadaveric glenoid bone, developed and utilized a system for loading the implanted specimens for 100,000 cycles to represent in vivo service, and performed high resolution optical and radiographic imaging of the specimens at various stages of loading in order to characterize micro-cracking and implant loosening. We have identified characteristics of crack initiation and progression in the cement mantle that interfaces the implant with bone. Additionally our data also shows a trend that the novel posterior step implant leads to earlier and more cement cracking, but neither the posterior step nor standard implant exhibit gross implant loosening after 100,000 cycles of loading. We have made the following progress related to each of the three Specific Aims:

*Specific Aim 1:*

We successfully designed and built a mechanical loading apparatus consistent with our research strategy. This apparatus applies mechanical loads in the anterior-posterior direction to glenoid

implants, similar to loads experienced in the real shoulder. Controlled forces and displacements are applied along two different axes. The apparatus includes a pneumatic actuator, load sensors, linear bearings, a custom machined carriage and clamp that holds the implanted specimen, and metal framing, all integrated with an existing servo-hydraulic linear actuator.

We implanted 2 synthetic bone specimens and 5 cadaveric human bone specimens with glenoid implants. We found that the synthetic bone specimens appeared to be an unrealistic representation of the real cadaveric human bone (see Aim 3), and thereafter focused on testing implanted cadaver glenoids. The cadaver specimens were much more expensive to obtain, and more cumbersome to test, but we believe this testing gave us very reliable, realistic data that is very translatable to clinical practice. Seven implanted specimens were successfully tested to completion.

Two different types of glenoid implants were tested, including one existing standard commercial 3-pegged UHMW polyethylene glenoid (Zimmer, Warsaw IN), and the novel posterior step implant. As part of this project we developed a revised approach for custom fabricating our posterior step implant. The posterior-augmented implants were prototypes that were fabricated by attaching a 5 mm thick custom-made polyethylene block to the posterior half of the pegged commercial implants. In our first experiment with this prototype we observed early failure of the adhesive bond that was connecting the block to the commercial implant. Thereafter we devised a new method for this attachment, specifically we fabricated dowel pins and corresponding holes that together served as a mechanical interlock between the block and commercial implant. These new prototypes did not fail in the remaining tests. We also refined the methods used to implant this implant into bone.

We successfully developed an approach for micro-CT scanning the implanted specimens at various stages of cyclic loading up to 100,000 cycles, and analyzing these scans in 3D with direct comparison among all time points. Each loaded specimen was subject to at least 6 full scans. All scans of a given specimen were co-registered together, and the evolution of cement cracking was quantified.

*Specific Aim 2:*

We successfully quantified toggle displacement of the anterior and posterior glenoid rims for all loaded specimens. A novel setup was devised for acquiring high resolution (~0.005 mm pixel size) digital images of the implant rims while the glenoid implant was being statically loaded with our custom apparatus. At 0, 1000, 10000, 25000, 50000, and 100000 cumulative cycles, photographs (macro lens; 5 mm/pixel) were recorded of anterior and posterior implant rims while eccentric loading was applied. Distances between marks located on the implant and bone potting were determined and toggle micromotion (implant loosening) and subsidence were calculated.

*Specific Aim 3:*

As mentioned above we successfully implemented our experiments in cadaver specimens in addition to synthetic bone substitutes. We found that the synthetic bone specimens fatigued earlier than the real cadaveric human bone: using micro-CT we observed plastic deformation of

the material, leading to substantial migration of the cement mantle and gaps forming at the implant-cement interface. We decided to focus on testing cadaver testing as described above.

The detailed Methods and Results are described below.

C. Methods:

*Design, fabrication, and troubleshooting of experimental cyclic loading machine*

For this project we designed and constructed a machine that applies controlled combined loadings to glenoid implants. These loadings simulate physiologic "high load" activities of the shoulder, such as lifting an item up onto a shelf. Fig. 1a shows a schematic of the loads applied, and Fig. 1b shows the constructed apparatus. The glenoid prosthesis is shown implanted into cadaveric glenoid bone. A humeral head prosthesis is welded to a steel arm, and this arm is fastened to a load cell (force sensor) which is fastened to the vertical actuator of our laboratory's servo-hydraulic mechanical testing machine (Interlaken/MTS, Eden Prairie MN). Two fundamental loads are applied to the glenohumeral joint (Fig. 1a): a vertical cyclic displacement, and a horizontal constant compressive force. The vertical cyclic displacement has a magnitude of +/- 2.5 mm relative to the joint-centered position, a frequency of 1 Hz, and is controlled by the Interlaken/MTS machine. The specimen is oriented such that these displacements are in the anterior and posterior direction of the glenoid. The glenoid specimen is fastened to a carriage that rides on a horizontal linear bearing. Two additional linear bearing units are attached to the humeral head side of the device in order to prevent bending loading of the vertical actuator rod.

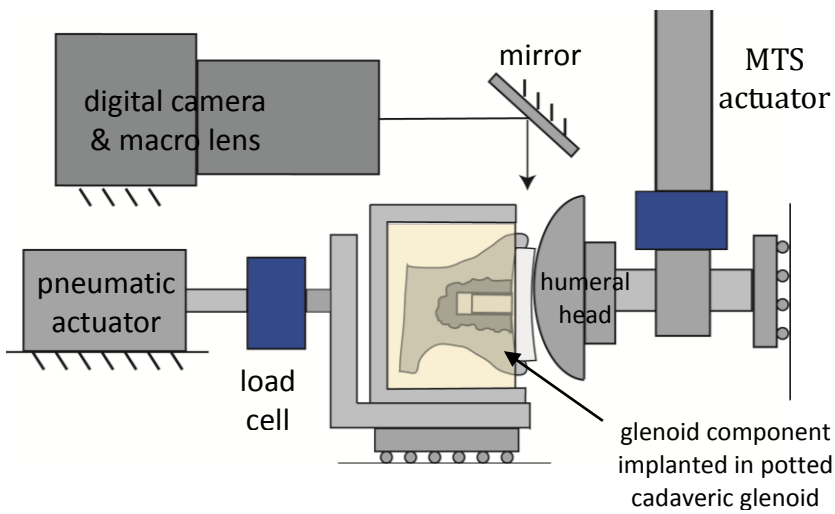



**Figure 1a** – schematic of loading apparatus

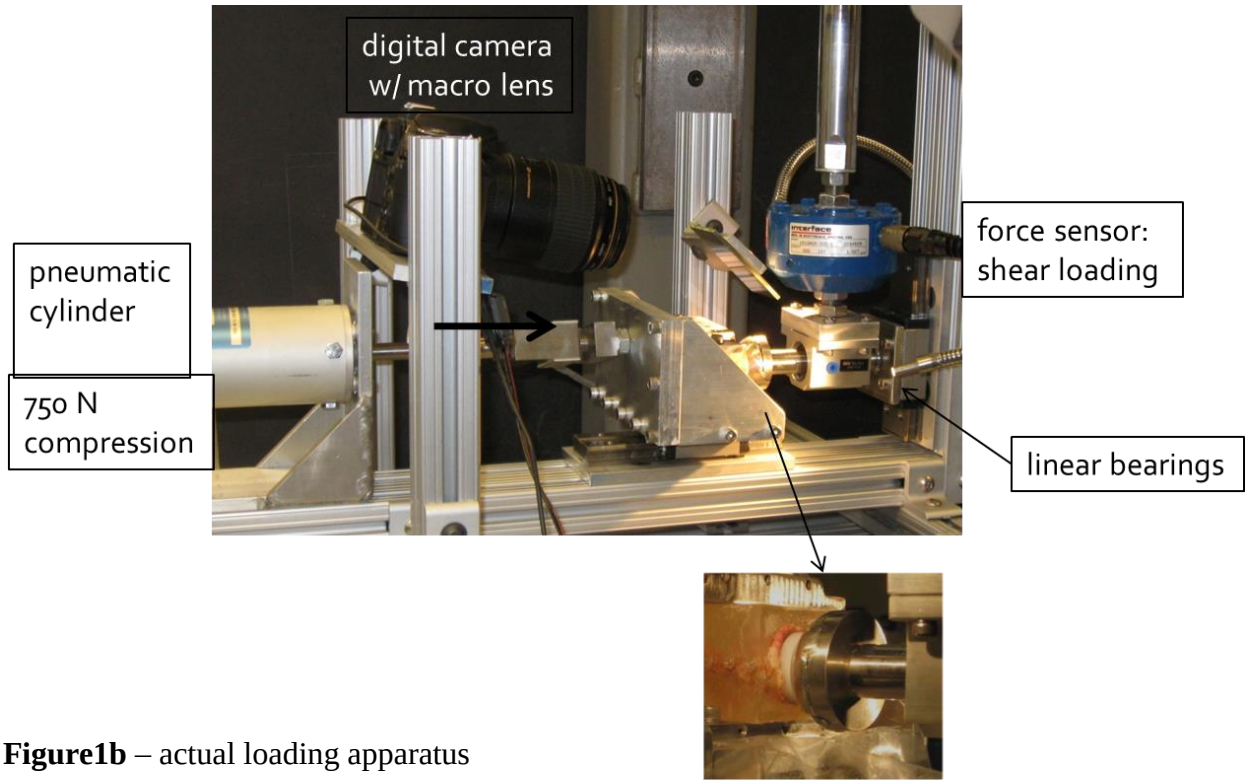



**Figure1b** – actual loading apparatus

The horizontal compressive force has a magnitude of 750 N and is applied by a pneumatic cylinder. The pneumatic pressure is held constant (~41 psi) by a pressure regulator, and actuator friction is minimized by using a rolling diaphragm cylinder with ball bearings (ControlAir, Amherst NH). This pneumatic system enables us to hold the horizontal force nearly constant (+/-5 N), as the glenoid carriage slides back and forth during cylic loading. The horizontal force is continuously monitored by a strain-gage based load cell, which is calibrated beforehand using stacked weights. For cadaver bone tests, before prosthesis implantation, the glenoid bone is potted in a rectangular block shape for later gripping by the loading apparatus. We fabricated an aluminum mold box, which includes a series of set screws for holding the bone in place (Fig. 2a,b,c). The glenoid is positioned with its face orthogonal to the box sides, and acrylic cement (Lang Dental, Wheeling IL) is poured into the box and cures at room temperature.

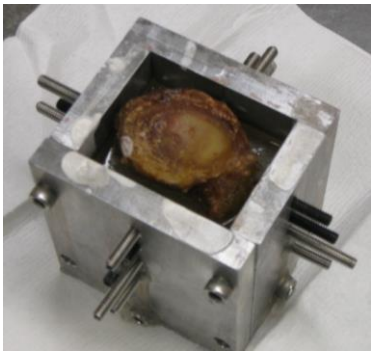
A  B C

Figure 2 a – aluminum mold box 2b – potted cadaver glenoid 2c – implanted step component

Implants: 2 types of glenoid implants were tested: (1) a standard commercial 3-pegged UHMW polyethylene glenoid (Zimmer, Warsaw IN); and (2) a novel posterior-augmented implant.

Specimen implantation: 2 specimens (S1 & S2) were implanted with the standard components, and 3 specimens (PA1, PA2, and PA3) were implanted with the posterior-augmented components.

Mechanical loading: Cyclic mechanical loads were applied using the custom device consistent with the ASTM standard for assessing glenoid loosening. A total of 100,000 cycles were performed, representing 25 high-load shoulder movements per day for ten years.

Toggle micromotions: At 0, 1000, 10000, 25000, 50000, and 100000 cumulative cycles, photographs (macro lens; 5 mm/pixel) were recorded of anterior and posterior implant rims while eccentric loading was applied. Distances between marks located on the implant and bone potting were determined and toggle micromotion (implant loosening) and subsidence were calculated.

Micro-CT analysis: Micro-CT imaging was also performed at the above 6 intervals using a vivaCT 40 (Scanco Medical, Brüttisellen Switzerland). Images were filtered and resampled to 38 mm voxels in Matlab. Image volumes from each time point were three-dimensionally co-registered with the before-loading images (Avizo, VSG US, Burlington MA) so that damage evolution could be visualized using multiple slicing directions. Cracks in the cement mantle around each peg were categorized as either through-mantle (crossing from implant to bone space) or partial-mantle.

D. Results:

We found the following results for the standard and posterior augmented implants. None of the implants exhibited gross loosening after the full 100,000 cycles. All implant toggle micromotions remained less than 1.0 mm (Fig. 3). In the majority of tests, greater than 75% of the final 100,000 cycle-micromotion was already present at 0 cycles (Fig. 3). Subsidence of the implant into the bone increased gradually during cycling. This amount of shifting exceeded 1.0 mm in 1 standard, and in 1 posterior augment implanted specimen (Fig. 4B). Interobserver

differences in micromotion measurements averaged < 0.05 mm. Micro-CT analysis revealed that internal damage in the cement mantles also gradually increased with cycling (Fig. 4C). Generally cracks first appeared small at stress concentrations, and then progressed to larger cracks. All cement cracks occurred at locations surrounding the upper half of the pegs (nearer to the glenoid face—Fig. 5); cement mantles deeper in the vault appeared undamaged. The posterior augment implanted specimens trended toward exhibiting more cement damage than the standard implanted specimens (Fig. 4C). Some failure of trabeculae occurred near the glenoid face (Fig. 5) and immediately surrounding the cement mantles.

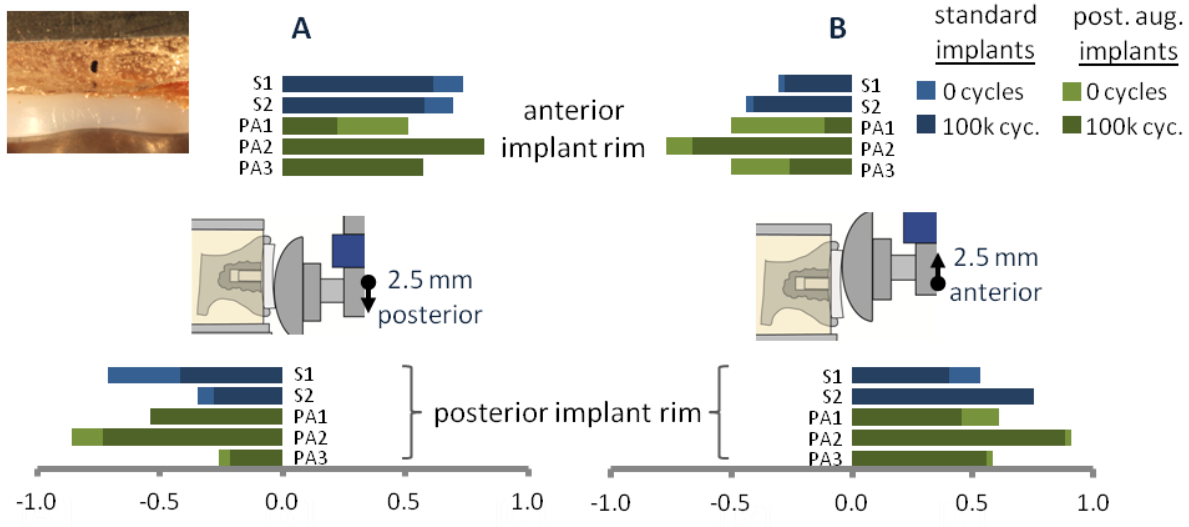



Figure 3: Toggle micromotions of the anterior and posterior implant rims during posterior [A] and anterior [B] static loading, at 0 and 100,000 cycles. Toggle micromotion was determined optically from the change in distance between markers relative to a centrally loaded condition.

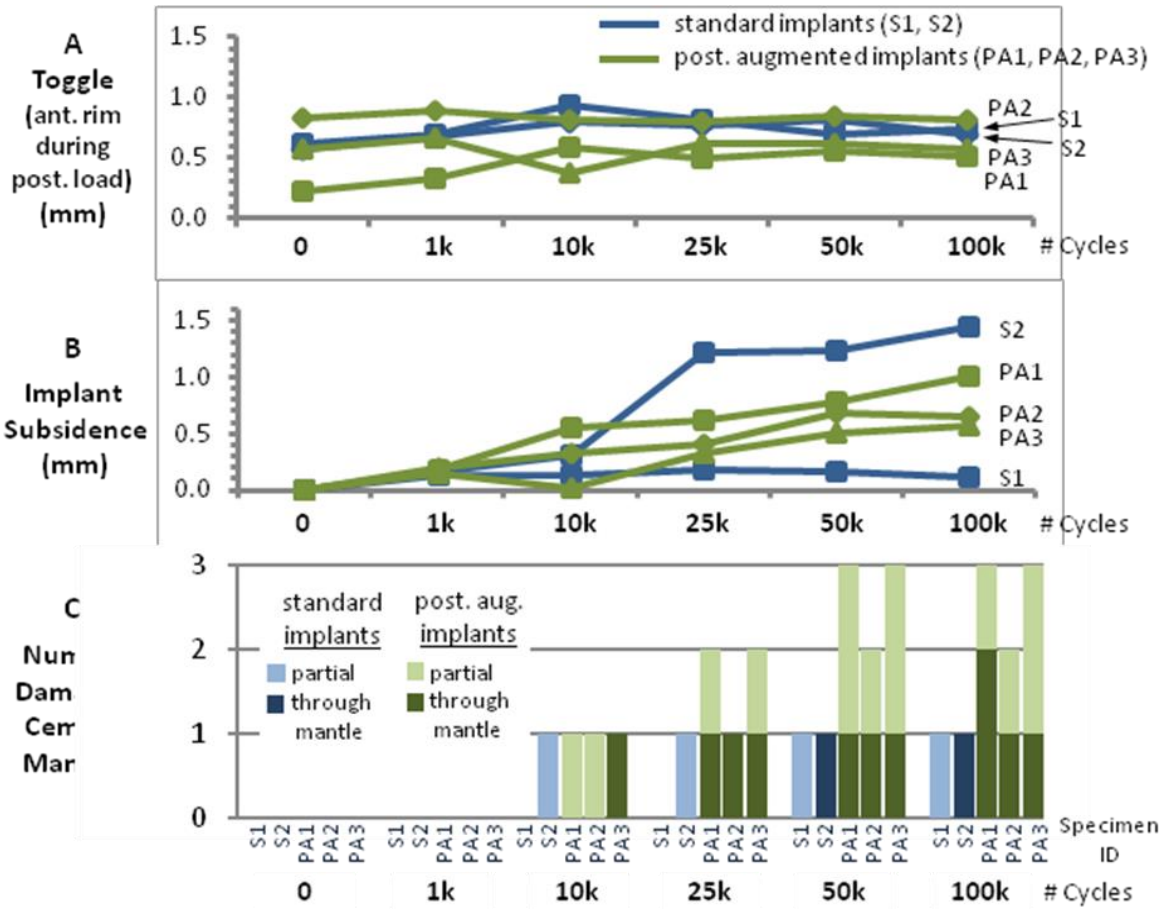



Figure 4: **[A]** Toggle micromotion, **[B]** subsidence of implant into bone, and [C] corresponding micro-CT assessed cement damage, at all time points. [B] Subsidence of the implant relative to the bone (potting) was determined from high-magnification photographs during central static loading. **[C]** Cracks in the cement mantle around each peg were categorized as either through-mantle (crossing from implant to bone space) or partial-mantle.

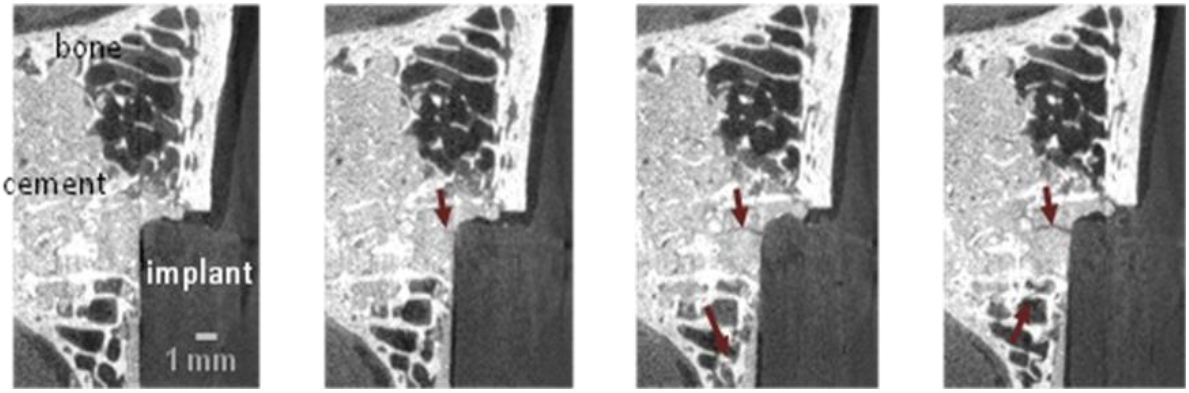



Figure 5: Co-registered micro-CT images of a posterior-augment implanted specimen at 0, 10000, 25000, and 100000 cycles (left to right). The added posterior step of the implant is visible in the bottom-right of the images. Progression of cement damage can be seen.

E. Conference Abstracts:

1. Lewis G, Brenza J, Paul M, Armstrong, A: Fixation Micromechanics of Cemented Glenoid Replacements. ORS 58th Annual Meeting, San Francisco, CA, February 4-7, 2012.

2. Lewis G, Brenza J, Paul M, Armstrong, A: Fixation Micromechanics of Cemented Glenoid Replacements. ASES Annual Closed Meeting, Sea Island, GA, October 11-14, 2012

3. Lewis GS, Brenza J, Paul E, Armstrong AD Implant micromotions and internal damage evolution in loaded cadaveric glenoids. Gordon Research Conference on Musculoskeletal Biology & Bioengineering, Andover, NH, August 2012.

We also used our developed methods as backing for a new R03 application submitted to the National Institutes of Health which was not awarded but was scored (roughly in top half of submissions).

**18. Extent of Clinical Activities Initiated and Completed**. Items 18(A) and 18(B) should be completed for all research projects. If the project was restricted to secondary analysis of clinical data or data analysis of clinical research, then responses to 18(A) and 18(B) should be "No."

18(A) Did you initiate a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
__X___No

18(B) Did you complete a study that involved the testing of treatment, prevention or diagnostic procedures on human subjects?

_____Yes
__X___No

**If "Yes" to either 18(A) or 18(B), items 18(C) – (F) must also be completed.** (Do NOT complete 18(C-F) if 18(A) and 18(B) are both "No.")

18(C) How many hospital and health care professionals were involved in the research project?

_____Number of hospital and health care professionals involved in the research project

18(D) How many subjects were included in the study compared to targeted goals?

_____Number of subjects originally targeted to be included in the study
_____Number of subjects enrolled in the study

**Note**: Studies that fall dramatically short on recruitment are encouraged to

provide the details of their recruitment efforts in Item 17, Progress in Achieving Research Goals, Objectives and Aims. For example, the number of eligible subjects approached, the number that refused to participate and the reasons for refusal. Without this information it is difficult to discern whether eligibility criteria were too restrictive or the study simply did not appeal to subjects.

18(E) How many subjects were enrolled in the study by gender, ethnicity and race?

Gender:
_____Males
_____Females
_____Unknown

Ethnicity:
_____Latinos or Hispanics
_____Not Latinos or Hispanics
_____Unknown

Race:
_____American Indian or Alaska Native
_____Asian
_____Blacks or African American
_____Native Hawaiian or Other Pacific Islander
_____White
_____Other, specify:_____
_____Unknown

18(F) Where was the research study conducted? (List the county where the research study was conducted. If the treatment, prevention and diagnostic tests were offered in more than one county, list all of the counties where the research study was conducted.)

**19. Human Embryonic Stem Cell Research.** Item 19(A) should be completed for all research projects. If the research project involved human embryonic stem cells, items 19(B) and 19(C) must also be completed.

19(A) Did this project involve, in any capacity, human embryonic stem cells?
_____Yes
__X__ No

19(B) Were these stem cell lines NIH-approved lines that were derived outside of Pennsylvania?
_____Yes
_____ No

19(C) Please describe how this project involved human embryonic stem cells:

**20. Articles Submitted to Peer-Reviewed Publications**.

20(A) Identify all publications that resulted from the research performed during the funding period and that have been submitted to peer-reviewed publications. Do not list journal abstracts or presentations at professional meetings; abstract and meeting presentations should be listed at the end of item 17. **Include only those publications that acknowledge the Pennsylvania Department of Health as a funding source** (as required in the grant agreement). List the title of the journal article, the authors, the name of the peer-reviewed publication, the month and year when it was submitted, and the status of publication (submitted for publication, accepted for publication or published.). Submit an electronic copy of each publication, listed in the table, in a PDF version 5.0.5 format, 1,200 dpi. Filenames for each publication should include the number of the research project, the last name of the PI, the number of the publication and an abbreviated research project title. For example, if you submit two publications for PI Smith for the "Cognition and MRI in Older Adults" research project (Project 1), and two publications for PI Zhang for the "Lung Cancer" research project (Project 3), the filenames should be:

Project 1 – Smith – Publication 1 – Cognition and MRI
Project 1 – Smith – Publication 2 – Cognition and MRI
Project 3 – Zhang – Publication 1 – Lung Cancer
Project 3 – Zhang – Publication 2 – Lung Cancer

If the publication is not available electronically, provide 5 paper copies of the publication.

**Note:** The grant agreement requires that recipients acknowledge the Pennsylvania Department of Health funding in all publications. Please ensure that all publications listed acknowledge the Department of Health funding. If a publication does not acknowledge the funding from the Commonwealth, do not list the publication.

| Title of Journal Article: | Authors: | Name of Peer-reviewed Publication: | Month and Year Submitted: | Publication Status (check appropriate box below): |
|---|---|---|---|---|
| 1. None | | | | ☐Submitted<br>☐Accepted<br>☐Published |

20(B) Based on this project, are you planning to submit articles to peer-reviewed publications in the future?

Yes_____x____ No_____

If yes, please describe your plans:

We are currently preparing a manuscript based on the above data and plan to submit our

paper to the Journal of Bone and Joint Surgery American, the most influential journal in orthopaedics. If the paper is not accepted we plan to submit to Journal of Shoulder and Elbow Surgery.

**21. Changes in Outcome, Impact and Effectiveness Attributable to the Research Project.** Describe the outcome, impact, and effectiveness of the research project by summarizing its impact on the incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of outcome, impact or effectiveness of the research project. If there were no changes, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

None

**22. Major Discoveries, New Drugs, and New Approaches for Prevention Diagnosis and Treatment**. Describe major discoveries, new drugs, and new approaches for prevention, diagnosis and treatment that are attributable to the completed research project. If there were no major discoveries, drugs or approaches, insert "None"; do not use "Not applicable." Responses must be single-spaced below, and no smaller than 12-point type. DO NOT DELETE THESE INSTRUCTIONS. There is no limit to the length of your response.

This cadaveric study is the first, to the best of our knowledge, to assess internal construct micro-damage in cemented glenoids subject to cyclic loading, and to correlate that damage with external measurements of implant loosening and subsidence. Implant toggle micromotions tended to not change substantially over time in response to anterior-posterior cyclic loading. Subsidence of the implant into the bone, on the other hand, increased steadily. Subsidence may be a better indicator of loosening-associated damage than toggle micromotion, although the latter is what is emphasized in current standards for glenoid implant testing. The posterior augmented implant tended to lead to more cement damage than the standard implant. However, toggle micromotions and subsidence were not markedly different, and the posterior augmented implant has the important advantage of restoring proper alignment with limited removal of healthy bone in difficult total shoulder arthroplasty cases. The study is limited by the lack of consideration of in vivo biological response such as bone remodeling.

**23. Inventions, Patents and Commercial Development Opportunities.**

23(A) Were any inventions, which may be patentable or otherwise protectable under Title 35 of the United States Code, conceived or first actually reduced to practice in the performance of work under this health research grant? Yes_____ No___x_____

If "Yes" to 23(A), complete items a – g below for each invention. (Do NOT complete items a - g if 23(A) is "No.")

a. Title of Invention:

b. Name of Inventor(s):

c. Technical Description of Invention (describe nature, purpose, operation and physical, chemical, biological or electrical characteristics of the invention):

d. Was a patent filed for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____

If yes, indicate date patent was filed:

e. Was a patent issued for the invention conceived or first actually reduced to practice in the performance of work under this health research grant?
Yes_____ No____
If yes, indicate number of patent, title and date issued:
Patent number:
Title of patent:
Date issued:

f. Were any licenses granted for the patent obtained as a result of work performed under this health research grant? Yes_____ No____

If yes, how many licenses were granted?_____

g. Were any commercial development activities taken to develop the invention into a commercial product or service for manufacture or sale? Yes___ No____

If yes, describe the commercial development activities:

23(B) Based on the results of this project, are you planning to file for any licenses or patents, or undertake any commercial development opportunities in the future?

Yes_____ No_____x_____

If yes, please describe your plans:

**24. Key Investigator Qualifications.** Briefly describe the education, research interests and experience and professional commitments of the Principal Investigator and all other key investigators. In place of narrative you may insert the NIH biosketch form here; however, please limit each biosketch to 1-2 pages.

## BIOGRAPHICAL SKETCH

| NAME | POSITION TITLE |
|---|---|
| Armstrong, April Dawn | Professor, Department of Orthopaedics and Rehabilitation |

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | MM/YY | FIELD OF STUDY |
|---|---|---|---|
| University of Western Ontario, London, Ontario | BSc | 06/92 | Physical Therapy |
| University of Western Ontario, London, Ontario | MD | 04/96 | Medicine |
| University of Western Ontario, London, Ontario | Residency | 06/01 | Orthopaedic Surgery |
| University of Western Ontario, London, Ontario | MSc | 06/02 | Hand and Upper Extremity Fellowship, Medical Biophysics |
| Barnes Jewish Hospital, Washington University, St. Louis, Missouri | Fellowship | 07/03 | Shoulder and Elbow Fellowship |

### A. Personal Statement

One of the major difficulties I encounter when implanting a total shoulder replacement, for arthritis, is with implanting the glenoid component. The glenoid vault is very small and quickly tapers off into a triangular-like shape and to make matters worse, in arthritis, the back of the glenoid (posterior portion) is worn away which further decreases the available bone for implantation. I started to look at other implant designs and started to investigate the concepts of step replacements to fill the void of the bone loss which were already being used for total knee replacements. Our first investigation into the concept of the posterior step glenoid component involved a biomechanical setup that measured 3D motion and cortical strains. The results were very encouraging for an all-poly posterior step component. We have more recently taken our investigation further by measuring the internal performance of the implant at the trabecular bone and cement interface under microCT. I am confident that Dr Lewis and I have the skills and knowledge to further develop our model and ultimately validate an FE model of the trabecular bone/cement/implant interface. This would have great clinical value in optimizing glenoid component design and implant techniques which would ultimately improve implant longevity. Dr. Lewis and I have worked together on a number of projects and we have aligned our research interests to continue to collaborate and advance the development of perimplant computer modeling.

### B. Positions and Honors

**Positions and Employment**

2003-2007 Assistant Professor, Orthopaedic Surgery, Department of Orthopaedics and Rehabilitation, Penn State Milton S. Hershey Medical Center, Shoulder and Elbow Reconstruction, Orthopaedics, Hershey, PA

2004-present Associate Director of the Division of Musculoskeletal Sciences, Department of Orthopaedics and Rehabilitation, Penn State Milton S. Hershey Medical Center, Hershey, PA

2006-present Director of Resident Research, Orthopaedics, Department of Orthopaedics and Rehabilitation, Penn State Milton S. Hershey Medical Center, Hershey, PA

2007-2013 Associate Professor, Department of Orthopaedics and Rehabilitation, Orthopaedic Shoulder and Elbow Reconstruction, Milton S. Hershey Medical Center, Penn State University College of Medicine, Hershey, PA

2013 – present Professor, Department of Orthopaedics and Rehabilitation, Orthopaedic Shoulder and Elbow Reconstruction, Milton S. Hershey Medical Center, Penn State University College of Medicine, Hershey, PA

2010-present Surgical Care Chief Medical Officer, Penn State Hershey Medical Group Surgical Care, Penn State Milton S. Hershey Medical Center, Hershey, PA

**Honors**

2004 AAMC Early Career Women Faculty Award, Association of American Medical Colleges

2006 Young Clinical Investigators Award, Bone & Joint Decade, USA/Canada

2007 OREF Zimmer Career Development Award

2007 AOA Emerging Leaders Program (ELP), American Orthopaedic Association

2009 ASES Exchange Fellowship Program, American Shoulder and Elbow Surgeons

2011 Dean's Award for Excellence in Teaching

**C. Selected Peer-reviewed Publications**

1. Bryce CD, Pennypacker JL, Nikhil K, Paul EM, Hollenbeak CS, Mosher TJ, Armstrong, AD: Validation of three-dimensional models of in situ scapulae. J Shoulder Elbow Surg, Sept/Oct; 17(5):825-32, 2008.
2. Lewis G, Bryce C, Davison A, Hollenbeak C, Piazza S, Armstrong AD: Location of the optimized centerline of the glenoid vault; a comparison of two operative techniques using 3D computer modeling. JBJS (Am) May 2010;92:1188-1194.
3. Bryce C, Davison A, Lewis G, Flemming D, Armstrong AD: Two-dimensional glenoid version measurements vary with coronal and sagittal scapula rotation, JBJS (Am) Mar 2010;92:692-699
4. Bryce CD, Davison A, Okita N, Sharkey N, Armstrong AD: The critical threshold of posterior glenoid bone loss JSES 2010, 149(7):994-1002

5 Lewis G., Armstrong, AD: Glenoid spherical orientation and version, JSES, Jan 2011;20(1):3-11.

6 Budge M, Lewis G, Hollenbeak, CS, Coquia S, Flemming D, Armstrong AD: Comparison of standard two-dimensional and three-dimensionally corrected glenoid version measurements JSES, Jun 2011;20(4):577-83.

7. Kirane Y, Davison A, Sharkey N, Armstrong AD: Failure mechanisms of a posterior step design glenoid component. JSES 2012 Jan; 21(1) 105-115.
8. Song N, Armstrong AD, Li F, Niyibizi C. Multipotent mesenchymal stem cells from human subacromial bursa: potential for cell based tendon tissue engineering. Tissue Eng Part A. 2013 Aug 21.

## D. Research Support

**Ongoing Research Support**

"Development and Validation of Mechanobiological Computer Models Enabling Personalized Surgical Approaches", CTSI KL 2 Award Principle Invesigator - Gregory Lewis, Ph.D. Mentors: April D. Armstrong, M.D. and Henry Donahue, Ph.D. February 8, 2012. $351,122.00 over 3 years.

**Completed Research Support**

OREF Zimmer Career Development Award #07-006 7/01/2007 – 6/30/2009
"Failure Mechanisms of a Posterior 'step-design' glenoid component"
Principal Investigator – April Armstrong, MD Co-Investigator - Neil Sharkey, Ph.D.
$50,000.00

No Number Assigned (Armstrong) 7/26/2010-9/30/2011
Penn State University, Dean's Feasibility Grant
Biomechanical Failure and Loosening Characteristics of a Novel Posteriorly Augmented Glenoid Component
Principal Investigator - April Armstrong, MD Co- Invesigator – Gregory Lewis, PhD
$38,268.00.

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

| NAME | POSITION TITLE |
|---|---|
| Lewis, Gregory Stephen | Assistant Professor |

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | MM/YY | FIELD OF STUDY |
|---|---|---|---|
| Lehigh University, Bethlehem PA | B.S. | 05/99 | Mechanical Engr. |
| Pennsylvania State University, University Park PA | Ph.D. | 12/08 | Mechanical Engr. |
| Penn State College of Medicine, Hershey PA | Postdoctoral | 09/08 to 05/11 | Orthopaedic Biomechanics |

### A. Personal Statement

My research and education interests involve mechanics and materials in bioengineering and orthopaedic surgical treatments. In 2012 I was awarded a career development grant from Penn State's Clinical and Translational Science Institute, part of the NIH CTSA consortium, for studying the micromechanical environment surrounding orthopaedic implants. Most recently I was named the 2013 Mary Judith Tevethia Junior Faculty Research Scholar. In these efforts I am developing successful collaborations with clinicians, basic scientists, and engineers. My teaching responsibilities include being lead instructor for BioE 505 Bioengineering Mechanics, and organizing the basic science course for the resident program in Orthopaedics.

### B. Positions and Honors

**Positions and Employment**

2012-present Assistant Professor (tenure-track), Orthopaedics, Penn State College of Medicine
2012-present Graduate Faculty, Intercollege Program in Bioengineering

**Honors**

2010 Finalist, Annual Outstanding Postdoctoral Fellow Award, Penn State College of Medicine
2012 Penn State Clinical and Translational Science Institute KL2 Scholar Award
2013 Mary Judith Tevethia Junior Faculty Research Scholar

### C. Recent Peer-reviewed Publications

1. Armstrong AD and Lewis GS. (2013) Design evolution of the glenoid component in Total Shoulder Arthroplasty: rationale and impact on operative technique. JBJS Reviews (in press)
2. Lewis GS, Bryce CD, Davison AC, Hollenbeak CS, Piazza SJ, Armstrong AD. (2010) Location of the optimized centerline of the glenoid vault: a comparison of two operative techniques with use of three-dimensional computer modeling. The Journal of Bone & Joint Surgery (American Volume) 92(5):1188-1194.

3. Loiselle AE, Wei L, Faryad M, Paul EM, Lewis GS, Gao J, Lakhtakia A, Donahue HJ. Specific Biomimetic Hydroxyapatite Nanotopographies Enhance Osteoblastic Differentiation and Bone Graft Osteointegration. Tissue Eng Part A. 2013 Mar 19.
4. Lewis GS, Armstrong AD. (2011) Glenoid spherical orientation and version. Journal of Shoulder and Elbow Surgery. 20(1):3-11.
5. Kirane Y, Lewis GS, Sharkey NA, Armstrong AD. (2012) Mechanical characteristics of a novel posterior-step prosthesis for biconcave glenoid defects. Journal of Shoulder and Elbow Surgery. 21(1):105-15.
6. Bryce CD, Davison AC, Lewis GS, Flemming D, Armstrong AD. (2010) Two-dimensional glenoid version measurements vary with coronal and sagittal scapular rotation. The Journal of Bone & Joint Surgery (American Volume). 92(3):692-699.
7. Bryce CD, Davison AC, Okita N, Lewis GS, Sharkey NA, Armstrong AD. (2010) A biomechanical study of posterior glenoid bone loss and humeral head translation. Journal of Shoulder and Elbow Surgery. 19(7):994-1002.
8. Budge MD, Lewis GS, Schaefer E, Coquia S, Flemming DJ, Armstrong AD. (2011) Comparison of standard two-dimensional and three-dimensional corrected glenoid version measurements. Journal of Shoulder and Elbow Surgery. 20(4):577-83.
9. Loiselle AE, Paul EM, Lewis GS, Donahue HJ. (2013) Osteoblast and osteocyte-specific loss of Connexin43 results in delayed bone formation and healing during murine fracture healing. Journal of Orthopaedic Research. 31(1):147-54.
10. Lloyd SA, Lewis GS, Zhang Y, Paul EM, Donahue HJ. (2012) Connexin 43 deficiency attenuates loss of trabecular bone and prevents suppression of cortical bone formation during unloading. Journal of Bone and Mineral Research. 27(11):2359-72.
11. Immonen JA, Zagon IS, Lewis GS, McLaughlin PJ. (2013) Topical treatment with the opioid antagonist naltrexone accelerates the remodeling phase of full-thickness wound healing in type 1 diabetic rats. Experimental Biology and Medicine (in press)

**D. Research Support**

**<u>Ongoing Research Support</u>**

8KL2TR000126-02 Sinoway (PI) 01/02/2012 to TBD/2014
NIH Clinical and Translational Science Awards Program: Penn State CTSI
KL2 Award: Development and validation of mechanobiological computer models enabling personalized surgical approaches
Role: KL2 Trainee (Lead investigator on my project)

Junior Faculty Research Scholar Award Lewis (PI) 07/15/2013 to 06/31/2015
Pennsylvania Department of Health (CURE program)
Development and testing of a novel simulation technology for fracture treatment education
Role: PI

No number given Kim (PI) 07/01/2013 to 06/30/2014
Orthopaedic Research and Education Foundation: new investigator award
Biomechanical assessment of a novel humeral head anterior-offsetting technique for difficult shoulder arthroplasty with posterior instability
Role: Co-I (Leading mechanics/engineering aspects of project)