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TITLE: Pathomechanics of Post-Traumatic OA Development in the Military Following Articular Fracture

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14. ABSTRACT The objective of the proposed research is to develop new models for predicting the risk of post-traumatic osteoarthritis (PTOA) following intra-articular fracture (IAF) by examining pre- and post-treatment CT data from patients with combat-related IAFs to measure fracture severity and post-reduction contact stress exposure. This study is being conducted in collaboration with the University of Iowa (PI: Donald Anderson, PhD) who is conducting these calculations on patients identified at the U.S. Army Institute of Surgical Research. A total of 70 subjects were included in the study with 112 fractures. As of the end of the reporting period, the protocol is closed at the partnering PI site. Our partners at the U of Iowa continue to work on related efforts in civilian trauma patients to refine the measuring techniques. The military subjects have posed some unique challenges in terms of availability of radiographs required; however military and civilian trauma data combined still promise robust knowledge products.					
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Introduction:

The objective of this research is to develop new models for predicting the risk of post-traumatic osteoarthritis (PTOA) following intra-articular fracture (IAF). Our collaborators at the University of Iowa previously developed capabilities to predict PTOA risk from acute fracture severity (measured from pre-op CT) and chronic elevated contact stress (post-op CT) associated with IAFs, but more patient data are needed to make the risk models clinically useful. Prospective studies of PTOA development following IAFs face many challenges. Severe IAFs are not frequently seen in civilian practice, making it difficult to accrue sufficient numbers for clinical study. An added challenge is that in order to determine if a patient develops PTOA, they may need to be followed for years into the future, threatening subject retention. One of the attractive features of the CT-based measures of mechanical factors pioneered by the Initiating PI (Anderson) is that retrospective studies can include patients who were injured years in the past. Recent military conflicts, which unfortunately produced a substantial number of severe fractures, including IAFs, provide a unique opportunity to overcome these challenges and to honor the military personnel who sustained combat-related IAFs. Given their prevalence and severity, and the degree to which these injuries impact long-term function of injured service members, better methods to predict PTOA risk would benefit our current generation of new veterans, as well as future service members at risk for IAF.

Keywords:

Post-traumatic osteoarthritis, CT analysis, intra-articular fractures

Accomplishments:

What were the major goals of the project?

Below is the original SOW:

Specific Aim 1: Evaluate pre- and post-treatment CT data from patients with combat-related IAFs to measure fracture severity and post-reduction contact stress exposure	
Major Task 1: Regulatory Approval	Months
Subtask 1.1: Obtain local IRB	1-3
Subtask 1.2: Obtain HRPO approval	4-6
<i>Milestone #1: Regulatory approval received</i>	5-6
Major Task 2: Adapt CT Analysis Methods	Months
Subtask 2.1: Obtain representative CT studies	3
Subtask 2.2: Trial analysis methods with CT studies	1-3
Subtask 2.3: Modify analysis methods as needed	3-9
<i>Milestone #2: Co-author manuscript on methods to analyze combat-related IAFs</i>	9-12
Major Task 3: Subject Identification	Months
Subtask 3.1: Obtain potential subject list with demographic and injury data from DoDTR	7
Subtask 3.2: Screen available CT scans for requisite images for inclusion	8-12
<i>Milestone #3: Subject list finalized</i>	12
Major Task 4: CT Calculations	Months
Subtask 4.1: De-identified CDs compiled and express mailed from Site 2 to Site 1	9-13
Subtask 4.2: CT calculations for injury severity and post-reduction contact stresses	10-18
<i>Milestone #4: Co-author manuscript on fracture severity and post-reduction contact stress measures in patients with combat-related IAFs</i>	18-24

Specific Aim 2: Measure the occurrence of PTOA up to ten years following fracture reduction surgery	
Major Task 5: PTOA radiographic frequency	Months
Subtask 5.1: Identify radiographs for KL grading; multiple investigators do KL grading	9-14
<i>Milestone #5: Co-author paper detailing PTOA incidence and grading for patients with combat-related IAFs</i>	16-20

Specific Aim 3: Quantify the extent to which fracture severity and post-reduction contact stress predict PTOA	
Major Task 6: PTOA symptoms and quality of life	Months
Subtask 6.1: Identify subjects' contact information through DoD and/or VA sources	12-16
Subtask 6.2: Conduct prospective contacting of subjects for outcomes questionnaires	12-28
<i>Milestone #6: Co-author manuscript detailing symptoms and treatment timelines for patients with combat-related IAFs</i>	25-32
Subtask 6.3: Correlate CT-based analysis results with KL grade/PTOA status, questionnaire outcomes, and various radiographic results	28-32
<i>Milestone #7: Co-author manuscript detailing relationships between CT-based results and PTOA outcomes – PTOA risk model</i>	32-36

What was accomplished under these goals?

Major Tasks 1 and 3 are now completed.

During the prior quarterly reporting period:

Major Task 2 is completed except for the publishing of our findings. A manuscript describing analysis methods has been revised during this quarter, and it will be re-submitted soon.

Major Task 4 CT analysis tasks are completed. We have completed fracture severity analysis of 101 fractures incurred by active duty military to date. The PI site at U of Iowa has continued to analyze civilian intra-articular fracture cases, as well, with fracture energies having now been computed for over 300 fractures. Contact stress analyses have also been completed for IAFs of the tibial pylon, the subtalar joint, and the acetabulum in our civilian cohort. Manuscripts have been drafted and will soon be submitted.

Major Tasks 5 and 6 have presented challenges in our military cohort. We have screened hundreds of patient medical records and encountered challenges that were all expected, but not to the degree actually experienced. The remaining difficulties include 1) a lack of follow-up radiographs or other records to comment on OA status and 2) a lack of requisite CT imaging. The follow up issue is a DoD medical system limitation that the team continues to struggle with, but we are hopeful that adequate medical follow-up will eventually be obtained. Clearly, though, the obtaining of reliable follow-up outcome data in the patients we have been analyzing has proven to be our most difficult challenge.

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

Nothing to report.

How were the results disseminated to communities of interest?

- Abstract presented at the Limb Lengthening and Reconstruction Society annual meeting (July 2017, Park City, UT) and the Military Health System Research Symposium (August 2017, Orlando, FL).
- Abstract accepted for presentation at 65th Annual Meeting of the Orthopaedic Research Society, (12-11-2018)
- Abstract submitted for 2019 OARSI World Congress on Osteoarthritis (12-11-2018)

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

Not applicable

Impact

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

Nothing to report; however, the end result of this project will contribute to discipline of PTOA prediction based on CT metrics.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

Changes/Problems

Changes in approach and reasons for change

Nothing to report.

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

Nothing to report.

Changes that had a significant impact on expenditures

Nothing to report.

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

Not applicable.

Products:

Publications, conference papers, and presentations

Podium presentation: Limb Lengthening and Reconstruction Society annual meeting (July 2017, Park City, UT)

Podium presentation: Military Health System Research Symposium (August 2017, Orlando, FL)

The PI site reports manuscripts in progress.

Website(s) or other Internet site(s)

Nothing to report.

Technologies or techniques

Nothing to report from this site directly from these data. The CR analysis techniques previously described by Dr. Anderson will face specific required modifications as they are applied to military subjects due to the severity of the injury and multiple fractures typical of combat injuries.

Inventions, patent applications, and/or licenses

Nothing to report.

Other Products

Nothing to report.

Participants & Other Collaborating Organizations

What individuals have worked on the project?

Name: Jessica Rivera

Project Role: PI

Nearest person month worked: 0.60

Contribution to Project: MAJ Rivera serves as the site study PI on this research project for the study's partnering PI option. She will provide the necessary programmatic leadership, administrative oversight and support for all aspects of the proposed work to be conducted at ISR/SAMMC site, ensuring that personnel and departmental resources

are properly aligned to achieve the goals of this study. She meets with the study personnel and communicates with the partnering site on a regular basis to review planning and execution of the proposed project. Finally MAJ Rivera will be responsible for the preparation of technical reports, manuscripts, and other dissemination materials generated by this study.

Name: Allyson Corona
Project Role: Research Coordinator
Nearest person month worked: 6
Contribution to Project: Ms. Corona is responsible for the day-to-day operations of the study. She will be responsible for assisting compilation of radiographic images and chart abstraction. She will also assist with the preparation of all study related correspondence and technical reports, maintain research files and data, procure study supplies and coordinate all procurement requests through The Geneva Foundation, and ensure budgetary adherence.

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

MAJ Rivera separated from the military around the same time as the project's closure at this site.

What other organizations were involved as partners?

Nothing to report.

Special Reporting Requirements

COLLABORATIVE AWARDS: The Collaborating PI at U of Iowa (Dr. Donald Anderson) is submitting a separate progress report for that site.