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:** Allegheny-Singer Research Institute

2. **Reporting Period (start and end date of grant award period):** 01/01/2009 – 06/30/2010

3. **Grant Contact Person (First Name, M.I., Last Name, Degrees):** Rebecca E. Pfeifer

4. **Grant Contact Person's Telephone Number:** 412-359-3137

5. **Grant SAP Number:** 4100047623

6. **Project Number and Title of Research Project:** 01 – Analysis of Ulnar Collateral Ligament Reconstruction

7. **Start and End Date of Research Project:** 01/01/2009 – 06/30/2010

8. **Name of Principal Investigator for the Research Project:** Patrick J. DeMeo, 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:

   $ 43,224.64

   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
DeMeo	Principal Investigator	1%	3,001.70
Miller	Consultant	14%	14,235.92
Cook	Consultant	20%	13,680.00

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
Kuxhaus	Postdoc	20%
Brogdon	Graduate Student	10%
Motlagh	Graduate Student	50%
Druschel	Research Assistant	15%
Laot	Undergraduate Student	10%

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:
Healing of the Distal Bicep Tendon, Clinical and MRI Assessment	☐NIH ☐ Other federal (specify:_____) X Nonfederal source (specify: Ferguson Foundation)	March 2009	$7,500	$7,500
Quantification of Pronation/Suprination Blockage after Mason II Fractures	☐NIH ☐ Other federal (specify:_____) X Nonfederal source (specify: Integra Inc)	July 2009	$25,000	$25,000

The Ferguson grant was awarded to Christopher C. Schmidt, MD. The support was based on successful use of the elbow simulator and the research supported by the CURE funds.

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:

Two grants will be submitted to NIH to study elbow repair. One application will request funding to support ligament repair and the second will request support to study radial head replacement. The next application date is October 5, 2010.

A grant will be submitted to Major League Baseball requesting funding for both the experimental and computer modeling parts of the project. This application is due in September 2010.

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

The experimental parts of this research project will continue because the results apply to sports medicine, which is a major focus of the clinical practice. The computer modeling parts will continue if additional external funding is provided to support the researcher, Harold Cook, who is an expert in this area.

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	1	2	
Female			1	1
Unknown				
Total	**1**	**1**	**3**	**1**

	Undergraduate	Masters	Pre-doc	Post-doc
Hispanic				
Non-Hispanic	1	1	3	1
Unknown				
Total	**1**	**1**	**3**	**1**

	Undergraduate	Masters	Pre-doc	Post-doc
White	1	1	3	1
Black				
Asian				
Other				
Unknown				
Total	**1**	**1**	**3**	**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.

The performance of the work enabled the research team to expand it abilities in experimental and computational methods. The project led to collaboration with the University of Pittsburgh and the use of a robot.

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:

The project led to collaboration with the University of Pittsburgh and the use of a robot.

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:

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.

Physical Characterization: Specific Aim #1: Quantify the in situ behavior of the medial ulnar collateral ligament using a robotic elbow simulator that creates physiologic conditions in vitro. Attainment of two goals will lead directly to the successful achievement of this aim: first, the preparation, mounting and measurement of elbow specimens in the robotic simulator; and second, the in vitro quantification of the force associated with the strains of the entire ligament. With the realization of the two goals, the project will have a complete characterization of the stress-strain behavior of the ligament for the essential inference of its in vivo performance.

OVERVIEW

The research has achieved the two goals set out in Specific Aim #1. The first goal encompassed the measurement of elbow movement and tissue deformation. This goal has been completed and extended to the application of a second robotic simulator. The second goal incorporated the measurement of forces with measurements of strain in the robotic simulator. This goal has also been completed. Not only have forces applied across the ligament been measured, but an additional technique to combine the force measurements with recorded measurements has been developed.

BACKGROUND

The medial ulnar collateral ligament (mUCL) is frequently injured in throwing athletes due to overuse or extreme valgus load. In order to repair the ligament, reconstruction with a graft may be required. This graft will be tensioned during reconstruction and elbow flexion will affect graft tension. Thus, a preferred angle for surgical reconstruction may exist. Furthermore, rehabilitation protocols will impose varying strains on reconstructed tissues and the demands of

therapy should be understood. A clear understanding of the tension in the native ligament can help in the restoration of the native biomechanics of the elbow and ensure the desired initial tension to the mUCL during surgery.

The multi-bundle structure of the medial ulnar collateral ligament has been well documented. It is widely considered that the mUCL consists of three longitudinal bundles, anterior, transverse and posterior, The most substantial is the anterior bundle, which is the primary valgus stabilizer of the elbow. The anterior bundle is itself considered to have either two or three bands, the anterior, middle and posterior. It has been shown that the anterior band becomes taut in extension and the posterior band becomes taut in flexion. The tension in each band is unknown but is very relevant to mUCL reconstruction because one may want to tension grafts to recreate aspects of physiological behavior. The level of strain in each band is directly related to the tension, but strain is also uncertain, however. The strain, however, can be more readily determined. To compute the *in situ* strains, one must know the physiological slack length for each band, where the slack length is defined as the length with no load applied and at which the band begins bearing load. This length correlates with an angle of flexion at which the band carries no load and is referred to as the reference angle in this study. While previous studies identified the reference angles in the bands of the anterior bundle of the mUCL by visual observation, this work seeks to establish a method to find reference angles quantitatively and *in situ*.

MATERIALS and METHODS: SPECIFIC AIM 1, GOAL 1

The mUCL was exposed in ten cadaveric specimens, seven males and three females, with a minimum, maximum and mean age of 43, 89 and 62±8 years respectively. Each specimen extended from the midhumerus to the hand. Monofilament with a 36 kg proof strength was firmly sutured using whip stitches to the brachialis tendon. The monofilament was then connected through a pulley system of an elbow simulator to an hydraulic actuator.

One mm diameter steel markers painted black were attached with very small amounts of cyanoacrylate adhesive to the anterior and posterior bands of the anterior bundle of UCL in each specimen. Individual fiber bundles were observed and the markers were attached along fiber lines. Markers divided each band into three regional segments which in this study were identified as superior (proximal), middle and inferior (distal) regions. Specimens were kept moist with saline after marker attachment and throughout all experimental procedures.

The specimens were then moved through full flexion/extension cycles (average range of motion: 104±12°) in the elbow simulator at a frequency of 0.1 Hz via feedback control of the brachialis muscle. The motion of markers on the specimen was tracked by video motion analysis (Spica Technology Inc., Kihei, HI) at a frequency of 20 Hz, while elbow flexion angle was monitored with an inclinometer (X3Q, US Digital, Vancouver, WA). To precondition the specimen, each specimen underwent three trials and the third trial of the tests was selected for marker tracking. The flexion/extension angle recorded by the inclinometer was electronically time-synchronized with the motion capture system.

The distance between each adjacent pair of markers was quantified and the slack length of the ligament was initially chosen arbitrarily as the length of the segments at 60° of flexion. Strain in

each segment, defined by two adjacent markers of the anterior and posterior bands of the ligament, was calculated and the strain - flexion angle relationship in each segment of each band was stored electronically.

To determine if the strains were uniform along each of the anterior, middle and posterior bands, a two-way repeated-measure ANOVA analysis was performed on each band using flexion angle and segment location as independent variables and the maximum tensile strain as the output variable.

Visual observation of the bands during flexion/extension showed that some segments of the anterior band in flexion and some segments of the posterior band in full extension were in a buckled, non-load bearing state, as previously indentified by Callaway, Morrey *et al*. and Regan. As the elbow moved through a flexion-extension cycle, the computed strain was observed to remain constant over a small flexion angle range. In the anterior band, strain then gradually increased with extension and finally increased more rapidly. An opposite flexion/extension behavior was noted in the posterior band, in which the constant strain was followed by strain gradually increasing with flexion followed by rapidly increasing strain (see SPECIFIC AIM 1: Figure 2).

The load-elongation relationship of ligaments is well known. This relationship exhibits an inflection point where the slope is small and positive and the curvature is also positive. The strain-flexion relationship as measured between markers exhibited behavior similar to the known load-elongation behavior of ligaments. Given that the length of the ligament varied with flexion, that ligaments bore more load with increased length, and that the bands exhibited regional buckling, some portion of the ligament should have no strain during a flexion cycle. One can therefore expect that the strain in a plateau region will represent the "toe" region of stress-strain behavior. The flexion angle, the "reference angle", representing the slack length should be found in this plateau region.

A mathematical routine was developed using MATLAB (Mathworks©, 2009) to determine the reference angle. A Butterworth low-pass zero phase shift filter $(n = 5, F_c = 1\ Hz)$ was first applied to length vs. angle data to eliminate motion artifacts and high frequency noise. Mathematically, the inflection point must have a small positive slope, $y'(0)$, and a positive curvature, $y''(0)$. A curve-fitting procedure was implemented to find families of functions that conformed to the requirements. Goodness of fit was later evaluated by adjusted R^2 coefficients. In some cases, if more than one zero point met the criteria, the curve which yielded the highest R^2 value was chosen.

All possible reference angles were considered. Every point near the loading portion of the strain-angle curve from the plateau onward was tested as a possible origin for the curve fitting procedure (SPECIFIC AIM 1: Figure 4). Curves were truncated at 2% strain level to correspond to the known behavior of ligmants with small loads and then the curve fitting procedure was performed. For each plot, linear polynomials of orders n=3 and n=4 and exponential curves, $y = a(e^{bx} - 1)$, were fit to the data. The latter exponential function was chosen because it is widely used to fit to the stress relaxation data for soft tissue and the stress and strain in the ligament are directly proportional to the flexion angle.

The identification of the slack length in the segments of a band with plateau regions (shown in and SPECIFIC AIM 1: Figure 2) allows the computation of the strain in the remaining segments of the band if one assumes that the band behaves as a unit. The extent of the plateau region was also quantified, as identified by the magnitude of the slope and sign of the curvature. The beginning of the regions was designated at the point after which the curvature and slope were always negative and end of the region was demarcated by the point at which the slope exceeded 0.0005 (see
SPECIFIC AIM 1: Figure **6**).

RESULTS: SPECIFIC AIM 1, GOAL 1
For the ten specimens evaluated, the average reference angle for the anterior band was 73° with a standard deviation of 5.3°, and the average reference angle for the posterior band was 70° with a standard deviation of 6.2°. The mean reference angle for each band with their standard deviation has been summarized in
SPECIFIC AIM 1: Figure **8**.

The ANOVAs showed that strains in the segments of anterior and posterior bands were significantly different (p=0.03, F=3.46 for the anterior and p=0.025, F=3.89 for the posterior bands).

Variation in the length of the anterior and posterior bands at three angles of a full flexion-extension cycle is shown in
SPECIFIC AIM 1: Figure **1** and the strain vs. flexion angle curves for posterior and anterior bands are shown in SPECIFIC AIM 1: Figure 2. The differing strain-angle behavior of the two bands is clearly shown. As an immediate consequence of this opposition, the strain behavior is clearly localized throughout the ligament length. Furthermore, the presence of a plateau region in the strain-angle relationship is only observed in specific segments (SPECIFIC AIM 1: Figure 4). Once one segment of a band undergoes buckling, that band is no longer capable of bearing load and the reference angle for that segment can be interpreted as that of the entire band.

Figure 5 illustrates different curve choices for the strain vs. angle of the anterior band. It is notable that the exponential function can result in the best fit.

Table 1 presents the reference angle and adjusted R^2 values for the selected segment of each band which resulted from different curve fittings. Plateau regions could be identified in some segments of the anterior and posterior bands. The average length of plateau region shown in SPECIFIC AIM 1: Figure **6**, was 6.5°

Comparing mean adjusted R^2 values, the exponential provided the best curve fit. The difference between the reference angle predictions of different curves was about 1.5° for the anterior and 2° for the posterior fibers.

The anterior band in nine out of ten elbows had the toe regions in the middle-region segments, whereas the remaining elbow had the toe region in more proximal segments. All the curves were observed to have a consistent phenomenological behavior in which strain increased

monotonically with extension followed by a constant strain in the toe region and finally monotonically increasing again. Two of the posterior bands showed toe regions without preceding regions of smaller. The toe region, in seven out of ten specimens, located in the middle segments and in the other three, it was in proximal regions.

A sensitivity analysis for different cut-off strains varying between 0 to 3% (presented in SPECIFIC AIM 1: Figure **7** for the anterior band) showed that the difference between predicted reference angles were not significant.

DISCUSSION: SPECIFIC AIM 1, GOAL 1

This work is the first to track local strains in the mUCL and use mathematical criteria to quantify the angles at which the anterior and posterior bands of the ligament no longer carry load. This behavior may be due to location of the insertion and origin of each band relative to the functional flexion/extension axis. The statistical difference in the strains along the lengths of the bands shows that the mUCL behaves locally. This result is not surprising given that the origin extends medially-laterally on the epicondyle and the insertion spreads more anteriorly-posteriorly out along the ulnar joint line and then down the ulna along the sublime tubercle. The difference in shape of the footprints of the origin and insertion cause the ligament near the humerus to have constraints due to the adjacent soft tissue while the ligament near the ulna is constrained most by the underlying bone. Thus, these changes in geometry and in the type of adjacent tissue along the length of the ligament may cause the strains to be different along the length of the ligament.

The recomputed strains are shown in Figures 8 and 9 for posterior and anterior bands, respectively. The resulting values are plausible but actual load-deformation testing should be performed on each band to verify the behavior. Observation of the local tissue behavior during flexion/extension indicated that the tissue nearer the insertion on the ulna maintained some tension while midsubstance tissue closer to the middle of the ligament's length and in the proximity of medial epicondyle buckled. The most lateral tissue closest to the trochlea, the tissue beneath the segments that buckled, also seemed to maintain tension. Testing of layers of the bands may also reveal the strains in the ligament to be localized by layer as well as by position along the ligment's length.

The results demonstrate the complexity of the mUCL. They are consistent and the method can be used in conjunction with testing with excised tissue to determine the stress-strain behavior. This study did not consider any anatomic variants. A larger number of specimens is clearly indicated so that anatomic variations can be considered.

The results are clinically significant in that they can be put to use during the reconstruction of the mUCL. If a single graft is used to augment both the anterior and posterior bands and if tension in the graft is uniform, then the flexion angle at which surgery is performed will bias the strains. For a single-bundle reconstruction, the current data suggest that the optimal elbow flexion angle at which to tension the reconstructed ligament lies between the optimal angle for each band, that is, 72° of elbow flexion. Current reconstruction surgical techniques put the arm in about 20° of flexion angle. It is obvious that in this angle, although the posterior band is in no-tension state, the anterior band is still taut and the ligament is experiencing some tensile stress. This study is

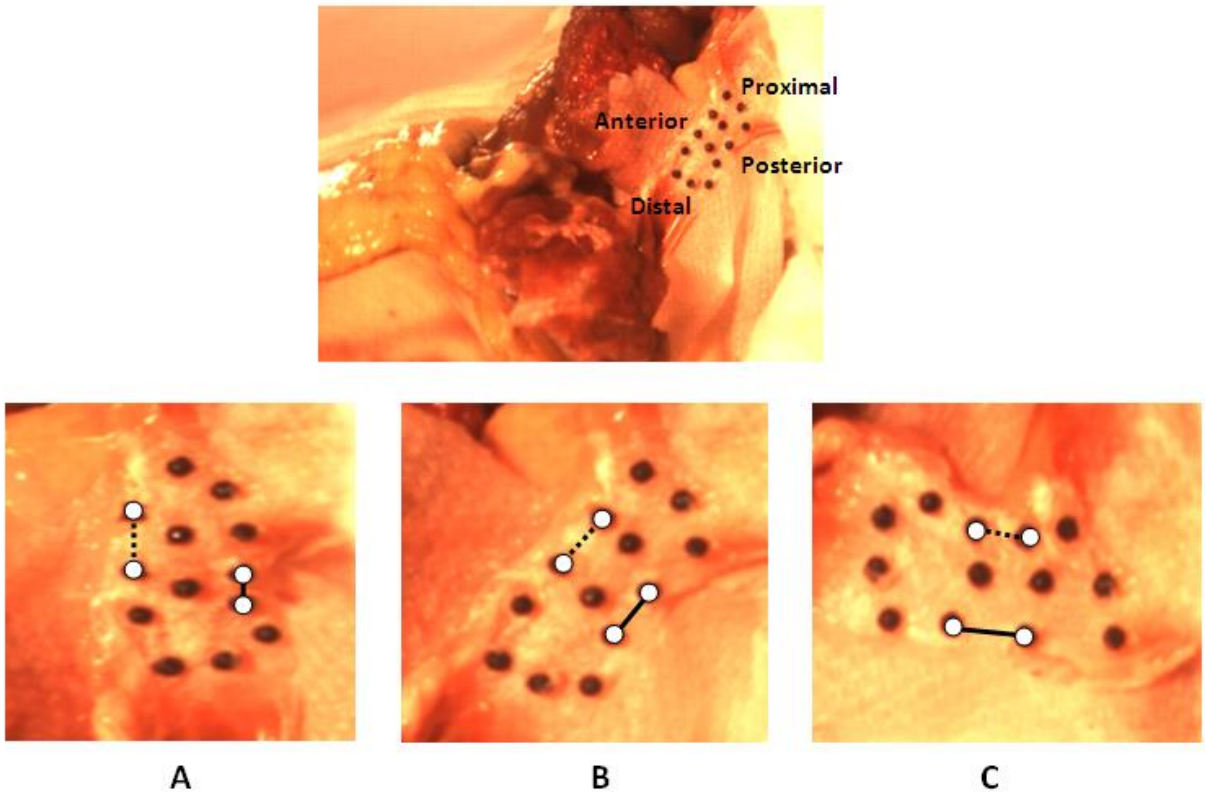
suggesting a new flexion angle where the arm could be positioned with minimum level of stress throughout the UCL.

RESULTS: SPECIFIC AIM 1, GOAL 2

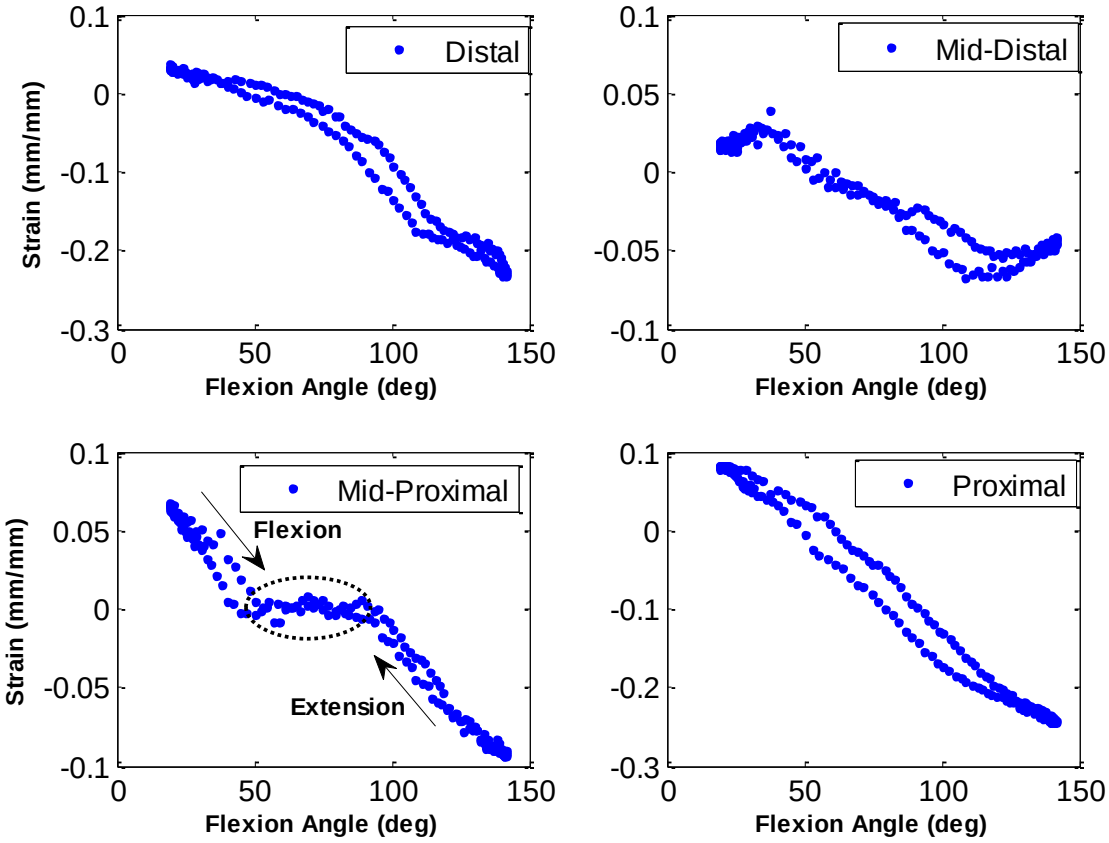
The forces applied to the mUCL were investigated using the 6-dof robot. The research originally was to use a uniaxial testing device with custom fixtures. However, the opportunity to use the robot arose after the research began; the robot offered a simpler means to achieve the same goal. One means to find the force in the ligament involves the use of the robot to establish the f/e path of passive motion. After recording the forces during the passive path movement, the ligament or parts of it are removed and the forces are again recorded during a passive movement. The difference in the recorded forces is the force experienced by the ligament. Figures 9 shows forces recorded during passive f/e movement.

The last aspect of the direct experiment work on the mUCL aimed to quantify the fiber direction of the ligament. Figure 10 shows a histological specimen of the mUCL obtained from the elbows tested in our laboratory. The fibers are evident and the direction can readily be quantified using standard software. Scientific histology for this work proved to be beyond the capabilities of the research assistant in the laboratory. Completion of quantitative histology would have required more funding than was available and was therefore postponed for future work.

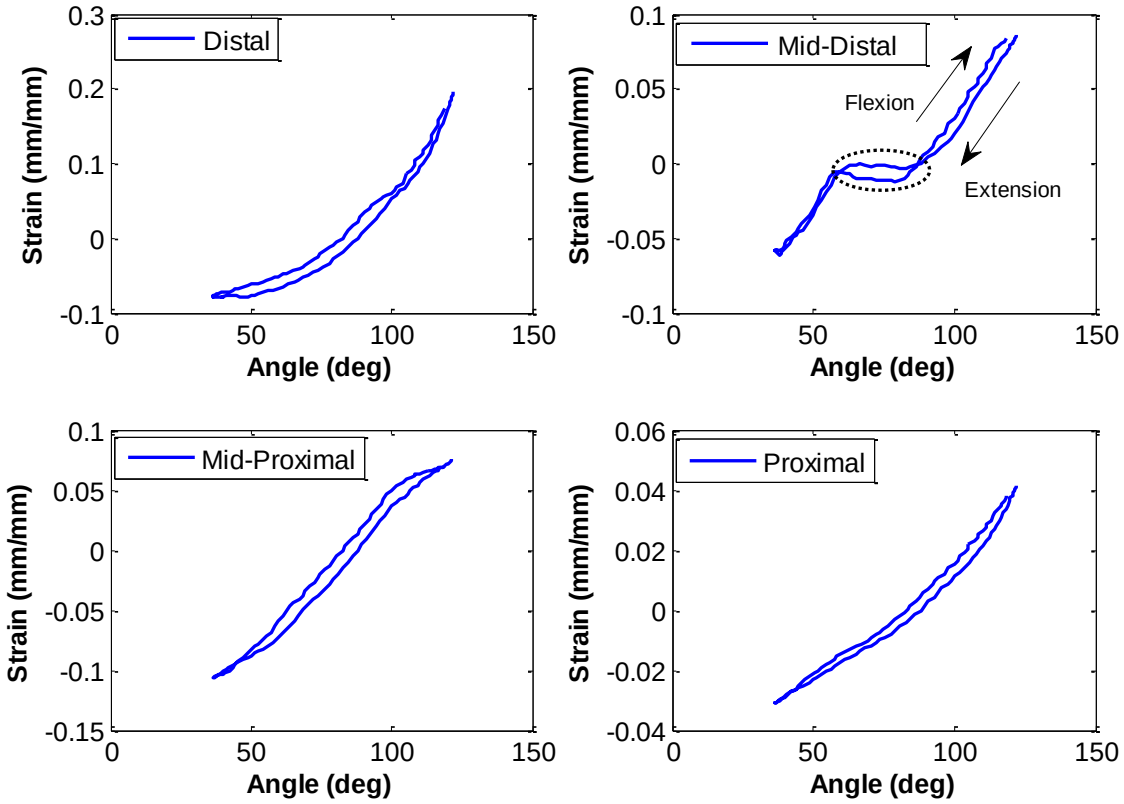
FIGURES and TABLES: SPECIFIC AIM 1



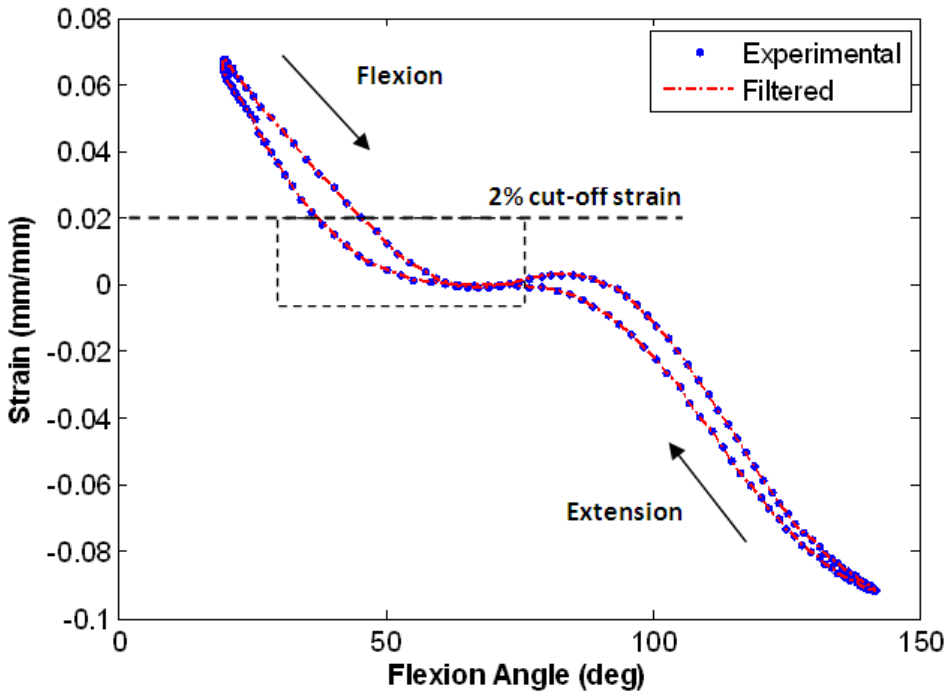
SPECIFIC AIM 1: Figure 1: Opposite segments strain (dotted line: anterior mid segment, solid line: posterior mid-segment) during A: full extension, B: 70° flexion angle (close to reference angle) and C: full flexion.



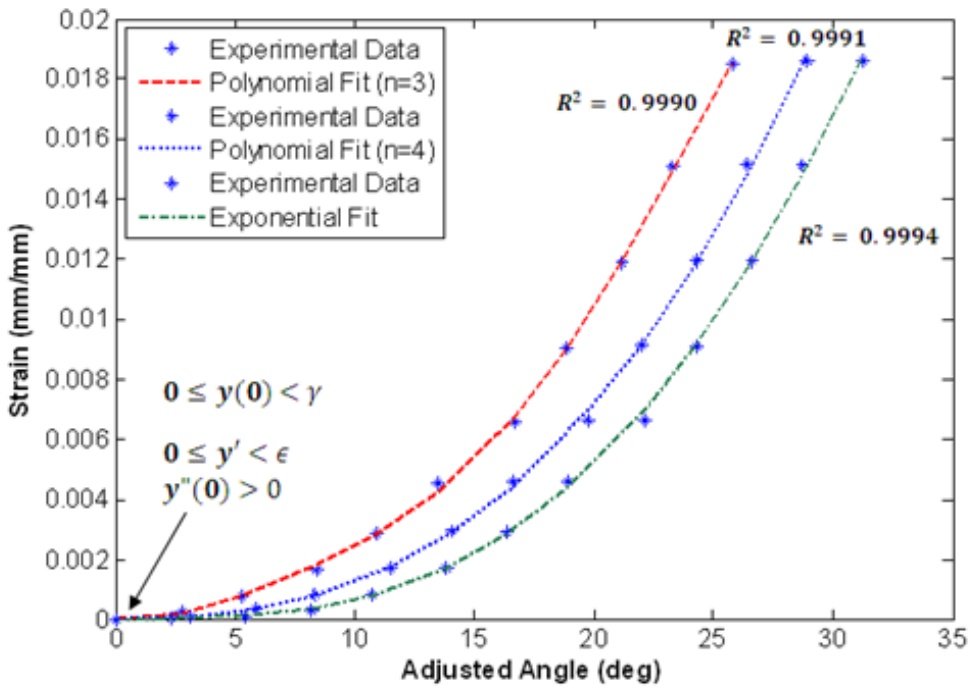
SPECIFIC AIM 1: Figure 2: Strain vs. flexion angle for different segments of the UCL *anterior* band (discussed toe region has been shown)



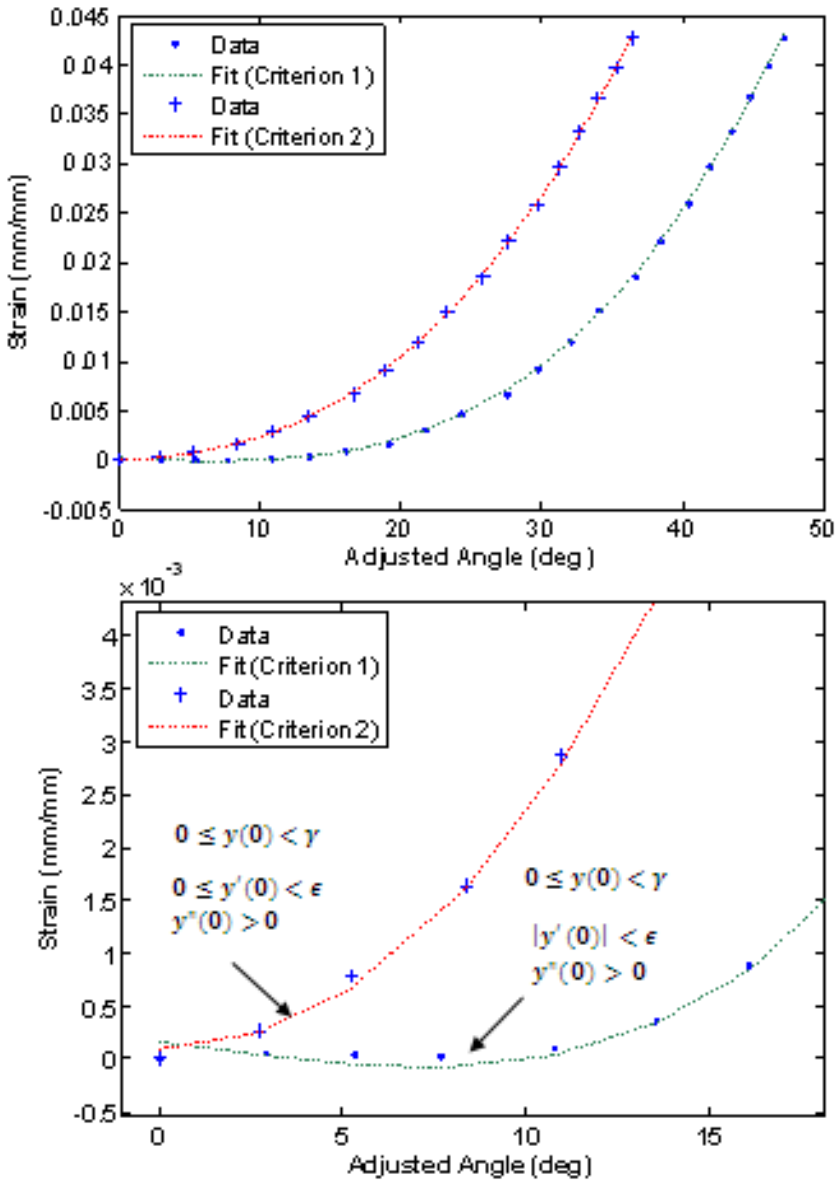
SPECIFIC AIM 1: Figure 3: Strain vs. flexion angle for different segments of the UCL *posterior* band



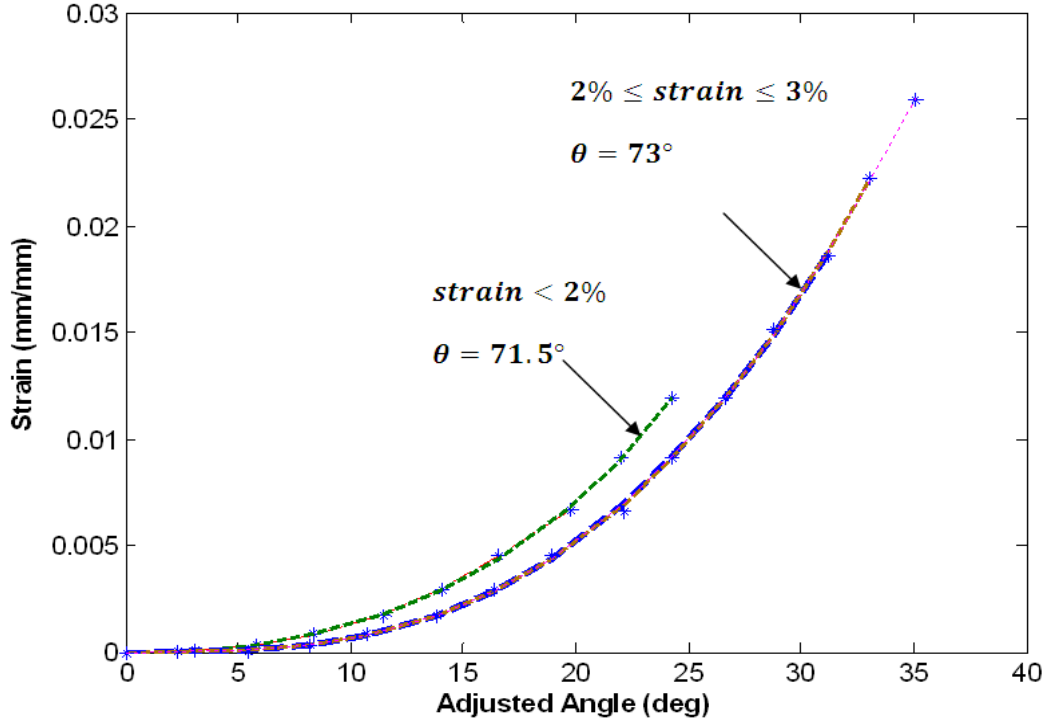
SPECIFIC AIM 1: Figure 4: Strain vs. flexion angle for one of the segments of UCL *anterior* band (curve fitting was implemented on the extension path within designated dotted region)



SPECIFIC AIM 1: Figure 5: Fitting different curves to obtain reference angles using criterion 2 (exponential function yields the best fit)



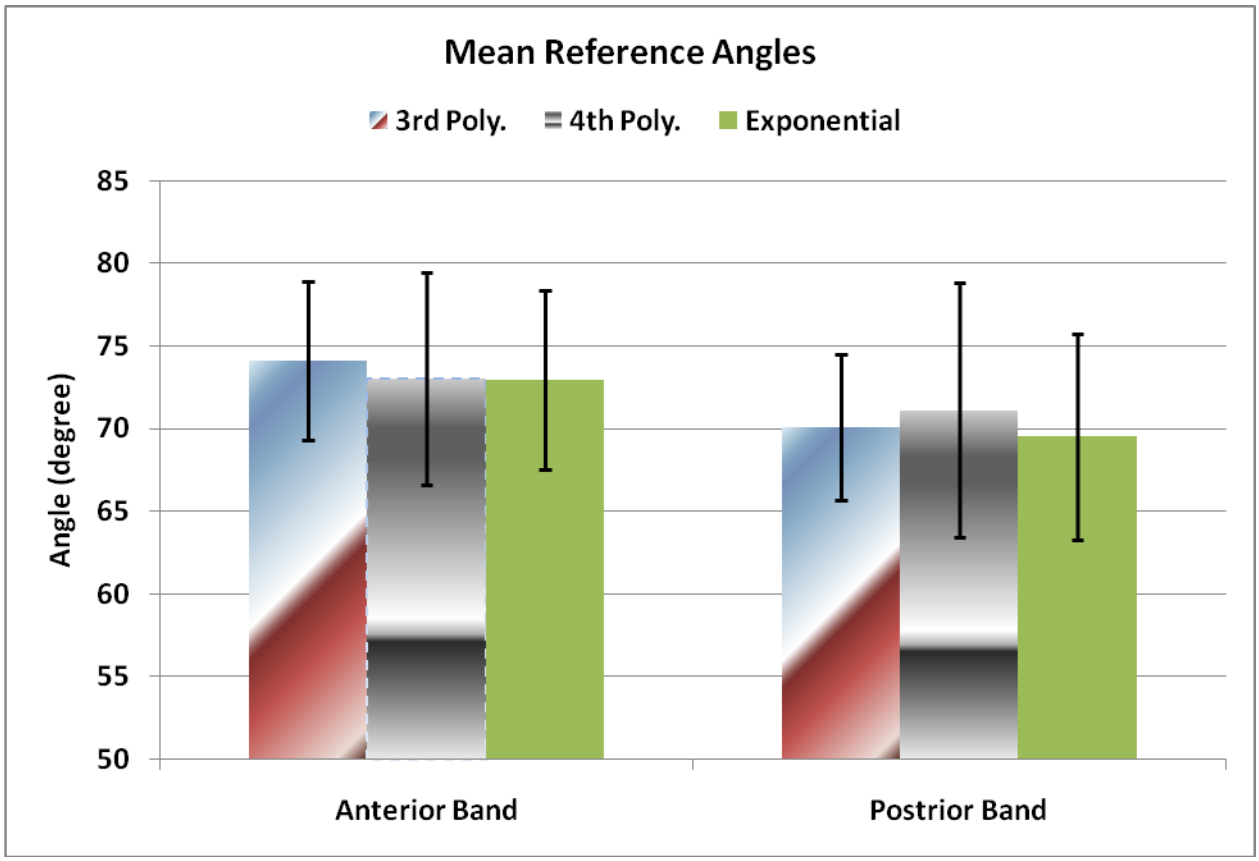
SPECIFIC AIM 1: Figure 6: comparing two criteria in predicting reference angles for a fifth order polynomial fit (top), a closer look to the curves in the vicinity of origin (bottom). Criterion 1 predicts smaller reference angles, because it allow negative slopes at the origin ($\epsilon = 0.0005 \; and \; \gamma = 0.0002$



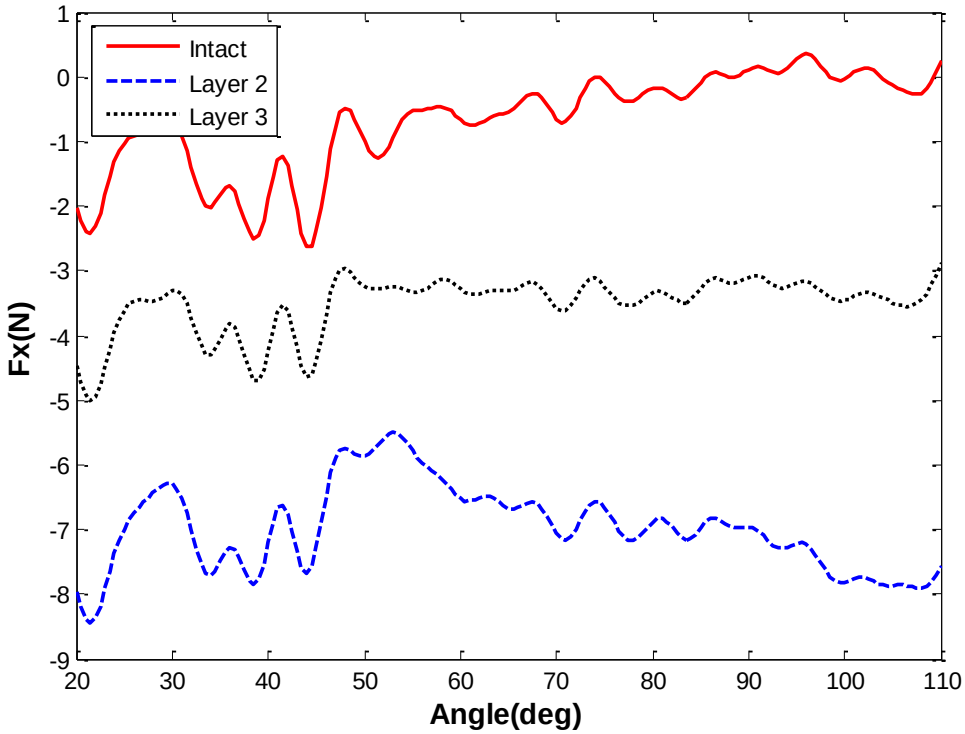
SPECIFIC AIM 1: Figure 7: Sensitivity analysis of the reference angle in anterior band for different cut-off strains in the curve fitting procedure

Band	Segment Location	Criterion	Curve Fit Functions											
			Polynomial (n=3)				Polynomial (n=4)				Exponential			
			Angle	Adj. R^2	y' (0)	y" (0)	Angle	Adj. R^2	y' (0)	y" (0)	Angle	Adj. R^2	y' (0)	y" (0)
Ant	Middle (9) Proximal (1)	1	67.5	0.979	0.00079	0.00035	66.3	0.990	0.00004	0.00012	69.4	0.994	0.00027	0.00002
		2	**74.1 (4.81)**	**0.980**	**0.00095**	**0.00036**	**73 (6.43)**	**0.991**	**0.00021**	**0.00016**	**72.95 (5.37)**	**0.996**	**0.00027**	**0.00002**
Post.	Middle (7) Proximal (3)	1	66.1	0.988	-0.00004	0.00025	64.5	0.988	0.00024	0.00004	66.2	0.993	0.00099	0.00003
		2	**70.09 (4.41)**	**0.989**	**0.00017**	**0.00026**	**71.13 (7.7)**	**0.988**	**0.00036**	**0.00012**	**69.51 (6.24)**	**0.995**	**0.00099**	**0.00003**

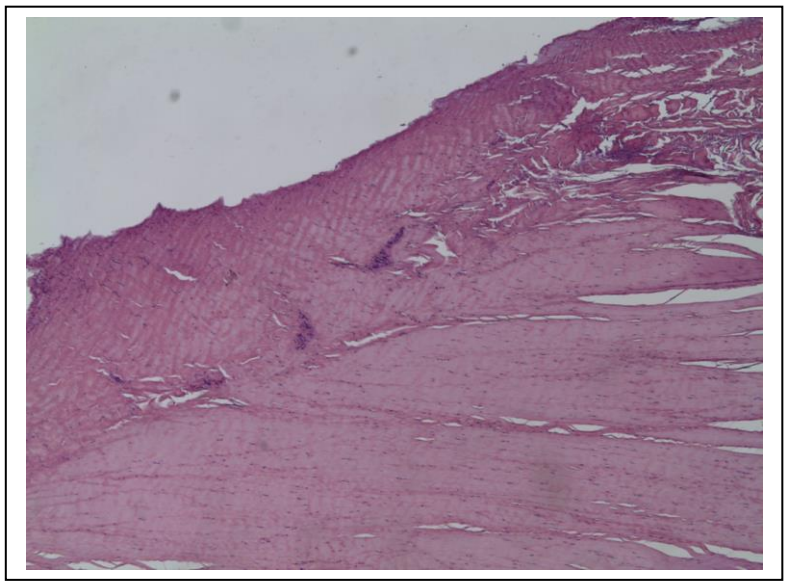
SPECIFIC AIM 1: Table 1: Summary of mean reference angles for ten specimens (bold numbers are reported, numbers in parentheses represent the standard deviations. All other numbers are mean values)



SPECIFIC AIM 1: Figure 8: Mean±SD reference angles for anterior and posterior bands



SPECIFIC AIM 1: Figure 9: Forces in the mUCL; the red line represents the total force before removal of the mUCL; black and blue lines represent the forces after tissue removal. The difference between the cases represents the force in the mUCL The data has been filtered to eliminate high-frequency noise.



SPECIFIC AIM 1: Figure 10: Histology for determination of the fiber direction of the mUCL

Mathematical Model –Specific Aim #2 A three dimensional model of the bones in a human arm will be created using CT data. From the CT scans, the geometry and the material properties of the bones will be determined. This model will be used to perform virtual UCL reconstruction surgery, with tunnels drilled in the ulna and humerus.

OVERVIEW: SPECIFIC AIM 2

UCL reconstruction surgery has been shown to have success rates as high as 90%, however there are still cases of complications. One particular complication is avulsion fractures of the humerus and ulna through the tunnels created for reconstruction. In this study we hypothesize the addition of these holes introduces a significant stress concentration in the surrounding bone. The aim of the study is to create a finite element model of the distal humerus and proximal ulna to study the stresses in the cortical and cancellous bone. Three separate models were created. In the initial model, the entire distal humerus was created from the CT scan of a donor arm. This model considered the bone stresses when the humerus was subjected to maximum muscle loads from the flexor/pronator group, but did not consider the loads from the ligament. The second model was of the proximal ulna from the same donor. This model studied the bone stresses in the sublime tubercle while varying the angular separation of the tunnels. The loading in this model was applied through the reconstructed ligament. The third model was a refined model of the distal humerus from a second donor arm. This model included muscle loading as well as loading from the reconstructed ligament.

METHODS: SPECIFIC AIM 2

In the first model, Mimics (Materialise, Leuven, Belgium) was used to segment the distal humerus. The geometry of the specimen was exported to 3D CAD software (Solidworks, Dassault Systems, Concord, MA). In addition to the native case, a virtual surgery was performed on the specimen simulating a modified Jobe reconstruction procedure. The diameter of the distal entry hole was set at 4.5mm and the diameter of the two converging proximal holes was set at 3.2mm. The entry hole was located slightly anterior of the center line of the medial epicondyle, and the medial-lateral location was varied ±2.25mm from the nominal position. The model was meshed in the finite element preprocessor LSPP (LSTC, Livermore, CA) and the resulting data returned to Mimics to have linear elastic, isotropic material properties assigned. Elements were either assigned as cortical ($E=17.5GPa$, $\nu=0.3$) or cancellous ($E=341MPa$, $\nu=0.3$) based on the value of the Hounsfield number. The average element edge length was 1mm at the medial epicondyle. For areas where the thickness of the cortical bone was less than 1mm (which included the entire medial epicondyle), shell elements were prescribed on the outer surface of the bone with a thickness of 0.75mm. The model was fixed around the proximal humeral shaft, and muscle loads from the flexor/pronator group which originate at the medial epicondyle were applied over their attachment areas. These muscle loads were calculated from the physiological cross sectional area and the maximum muscle stress and totaled 545N. The direction of the load was applied to simulate a 90 degree flexion angle. The palmaris longus muscle was excluded, as the tendon from this muscle is most commonly harvested to be used as the replacement ligament. The model was solved using the LS-Dyna FEA (LSTC, Livermore, CA).

In the second model of the ulna, a similar procedure was used to create the model. A virtual surgery was performed on the specimen simulating the docking procedure. The diameter of the ulnar tunnels was set at 3.2mm. The tunnels were positioned 3mm from the joint line. The

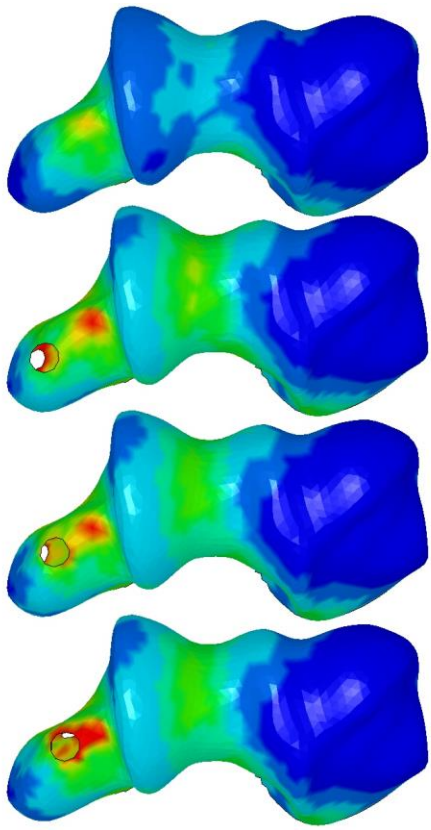
distance between the two entry holes was varied by changing the angle between the two tunnels. A radius of 1.5mm was constructed at the juncture of the tunnels to remove the sharp corner, and simulate connecting the tunnels with a curette, as described in the literature. The depth from the surface of the sublime tubercle to the top of the converging tunnels was held constant at 6.35mm. The ulna model was condensed to the sublime tubercle and a minimal amount of surrounding bone, as shown in Figure 1. The condensed model was then meshed in the finite element preprocessor LSPP (LSTC, Livermore, CA) and the resulting data returned to Mimics to have linear elastic, isotropic material properties assigned. Elements were assigned either cortical (E=17.5GPa, ν=0.3) or cancellous (E=341MPa, ν=0.3) properties based on the value of the Hounsfield number. An average element edge length of 0.75mm was chosen after a convergence study. The model was fixed along the truncated interior surface. The replacement tendon was modeled with linear elastic, isotropic elements. The tendon was modeled according to the docking procedure, so that the proximal ends of the tendon were directed toward the distal tunnel in the medial epicondyle. Contact elements were included between the tendon and the bone, and the tendon was free to slide in the tunnels. A displacement was applied to the tendon ends to simulate a moment of 14Nm, which was the maximum torque found in a biomechanical study of the modified docking procedure. The model was solved using the LS-Dyna FEA program (LSTC, Livermore, CA).

In the third model, a refined model of the humerus is considered. This model was created from the CT of a second donor arm (62 year old male). The procedure for creating the solid model varied from what had been done previously in that the Slicer program was used to segment the bones from the CT scans, and a custom Matlab program was used to assign the material properties. In this model, loading from the replacement ligament was considered along with the muscle loading. The load on the ligament bands was calculated from a 14Nm valgus torque, similar to what was done with the ulnar model. In this model of the humerus, smaller elements were used, and the cortical bone was modeled with solid elements rather than shell elements. Also, the ligament was tied to the interior wall of the tunnel and was not free to slide in the tunnel. This is meant to simulate the reconstruction after healing has occurred, and the ligament has attached to the bone.

RESULTS: SPECIFIC AIM 2

1) Preliminary Model of Humerus

SPECIFIC AIM 2: Figure 9 shows the results of the Von Mises stress distribution in the cortical shell elements for the native case as well as the three additional cases where the hole position was moved from the original site. The maximum stresses occurred in the distal aspect of the medial epicondyle. The stresses for the models simulating reconstruction are larger than the stress in the native case, as was expected. Although the maximum stress is similar among the three reconstructed models, moving the hole laterally toward the trochlea (where there naturally exists a larger stress, as shown in the case without holes) causes the volume of bone with higher stresses to increase. A medial hole placement also increases the stress above the central placement. The Table shows the maximum values of the stress for both the cortical shell and cancellous solid elements. In all cases, the calculated stresses are well below the yield stress for cortical (σ_y =115 MPa) and cancellous (σ_y =4.5MPa) bone.



Hole Position	Max Cortical Stress (MPa) [% of yield]	Max Cancellous Stress (MPa) [% of yield]
None	25.3 [22%]	1.55 [34%]
Medial	47.4 [41%]	2.63 [58%]
Nominal	49.7 [43%]	2.29 [51%]
Lateral	47.1 [41%]	2.73 [61%]

SPECIFIC AIM 2: Figure 10 - Cortical Stress in Initial Humeral Model

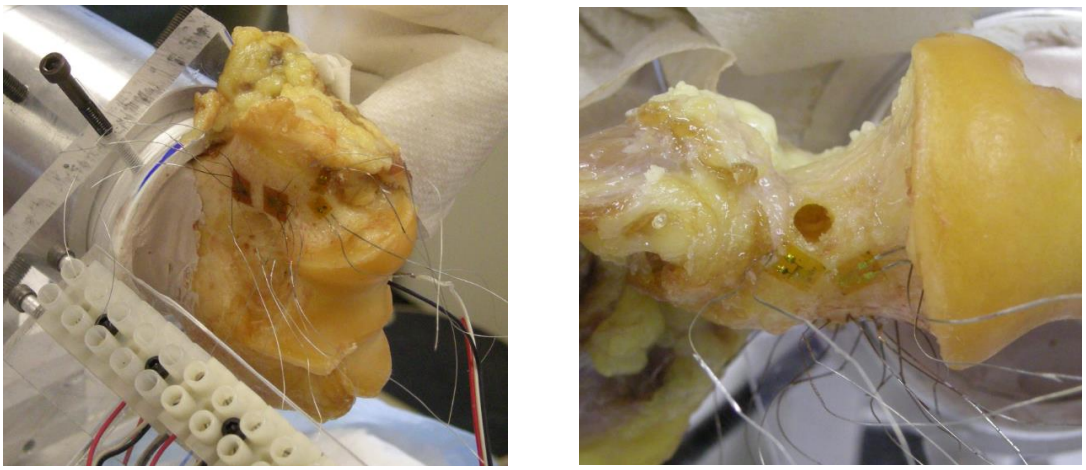
EXPERIMENTAL: SPECIFIC AIM 2

An experiment was conducted to verify the results obtained from the initial model, which only included the loading from the flexor-pronator muscle group. In this experiment, load was applied to the humerus through the muscles to replicate the loading condition in the finite element model. The humerus was removed from a cadaver specimen, keeping the entire flexor pronator muscles and distal tendons. The humeral shaft was attached to fixture that was free to move in the horizontal plane, which allowed the humerus to self-center under the applied tendon load. The humerus was oriented so that the load was applied at 90° of elbow flexion. A materials testing machine was used to pull on the distal tendons using a custom designed clamp with serrated faces. The load applied to the specimen was limited to 50% of the calculated maximum load in order to avoid damaging the specimen.

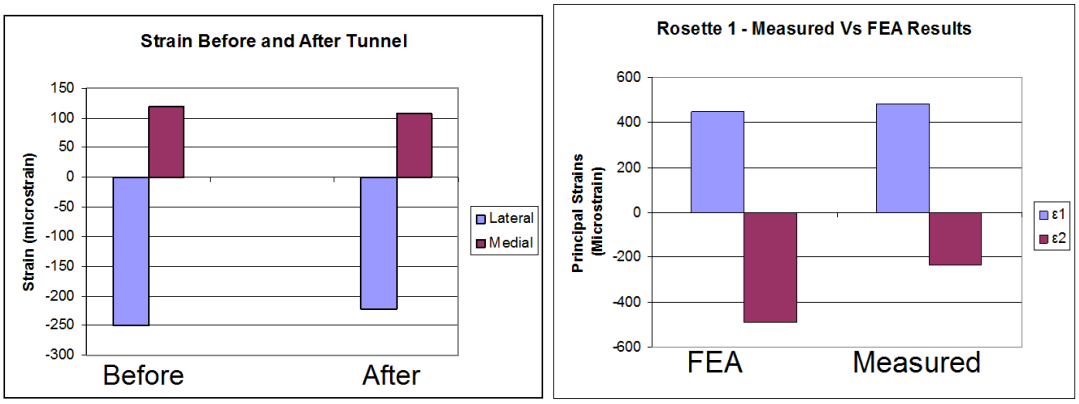
Two resistance strain rosettes were applied to the posterior surface of the medial epicondyle after thorough cleaning and drying. Two additional single element strain gauges were attached to the anterior edge of the medial epicondyle near the location where the humeral tunnel would subsequently be drilled. SPECIFIC AIM 2: Figure 12 shows the locations of the strain gauges on the specimens. The strain rosettes allow the principal strains and directions to be determined, and the single element gauges allow only the measurement of strain along the axis of the gauge.

Load, displacement, and strain measurements from the eight strain channels were recorded as load was applied.

SPECIFIC AIM 2: Figure 11 shows the results from this experiment. On the left, the strain in the single element gauges are shown before and after the tunnel was drilled. In this test the tunnel was drilled relatively far from the placement of the gauges, and as a result only a small change in the strain was measured. The graph on the right shows the comparison between the measured and calculated principal strains at the proximal strain rosette. The maximum principal stress match closely, however the measured minimum principal stress is approximately half what was calculated at the same position. In this study, the tested cadaver specimen was similar in size, but not the same specimen the FE model was created from.



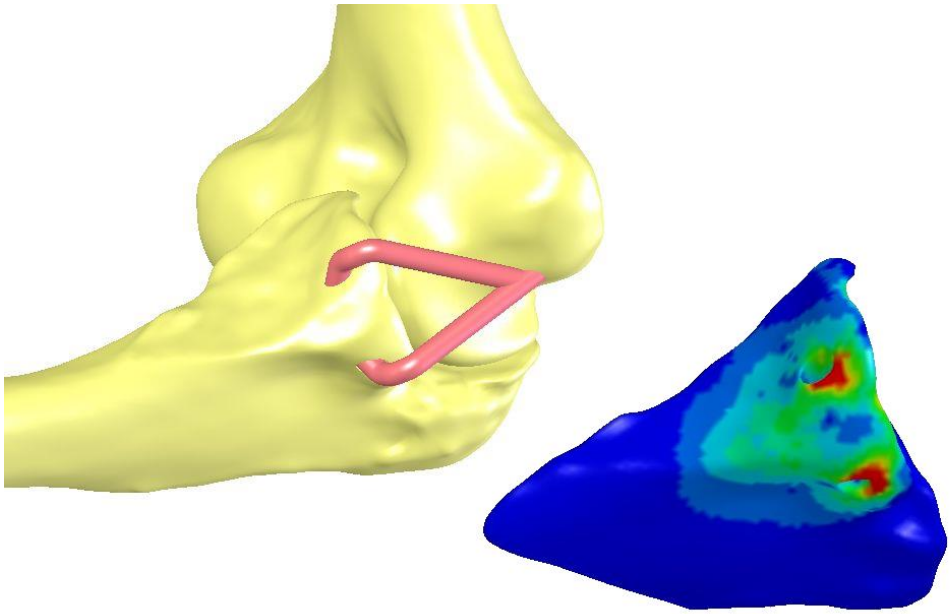
SPECIFIC AIM 2: Figure 12 - Photos of strain validation experiment. Strain gauges were placed on the posterior and distal ends of the medial epicondyle (left), results were compared between the native case and the case where a tunnel was created in the distal medial epicondyle



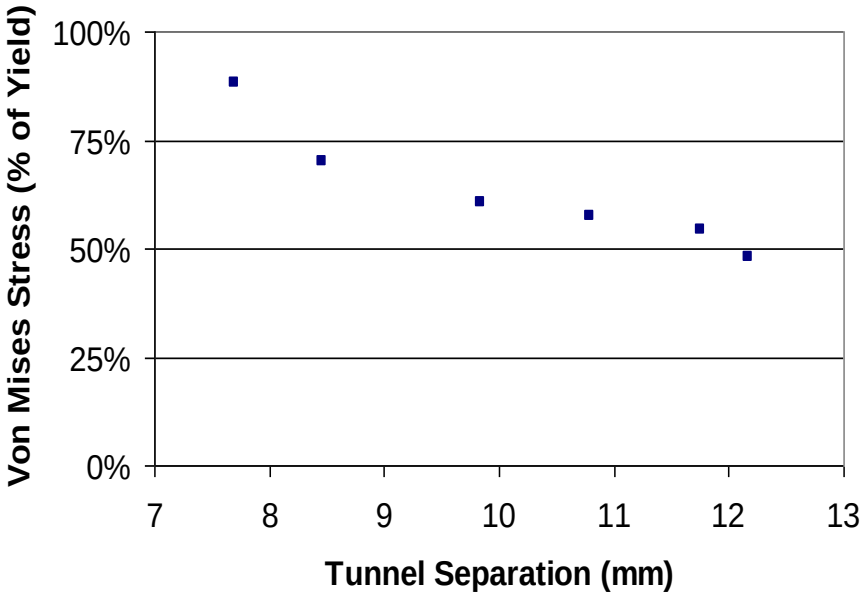
SPECIFIC AIM 2: Figure 13 Results from preliminary FE validation experiment. Strain in the single element gauges before and after humeral tunnel was drilled is shown on the left, and comparison between FE model and measured result at proximal rosette is shown on the right

2) PRELIMINARY MODEL OF ULNA

A contour plot of the cortical stress in the ulna is shown in SPECIFIC AIM 2: Figure 14. A graph of the maximum stresses in the cortical bone at either tunnel versus tunnel separation is shown in SPECIFIC AIM 2: Figure 15. The highest stress was at the edge of anterior hole when the separation was less than 10mm, and at the posterior hole when the separation was greater than 10mm.



SPECIFIC AIM 2: Figure 14 - Ulnar model



SPECIFIC AIM 2: Figure 15 - Maximum cortical stress v. tunnel distance

3) REFINED MODEL OF HUMERUS

Parameter Studies

In this model, several parameter studies were conducted to determine the sensitivity of each parameter and the best value of each parameter to use. In some of these studies, certain parameters had values that were not clinically relevant, but simulations using these values were instructive from a computer modeling standpoint. For example, in some of the studies the entire medial epicondyle was modeled as cancellous bone, although not clinically relevant it allowed clearer interpretation of the results than what would be obtained from a model with cortical and cancellous bone. The following sections outline the parameter studies.

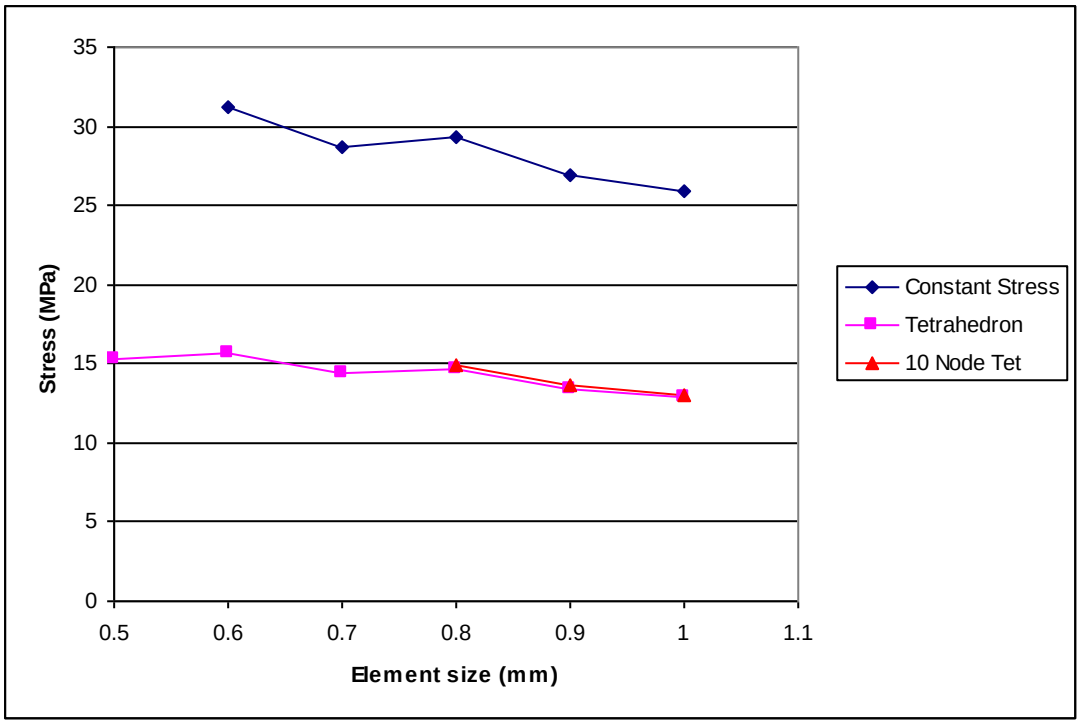
1) Effect of Varying Element Size and Element Type

Description: Fundamental to finite element analyses are the type and size of the elements used. The model is discretized into elements to represent the morphology of the bone, and we wish to find the largest element size that will accurately predict the stress in the model. This convergence study will attempt to find the correct element size to use by varying the element size (h-type convergence), or by varying the element type to a higher order element while keeping the FE mesh the same (p-type convergence).

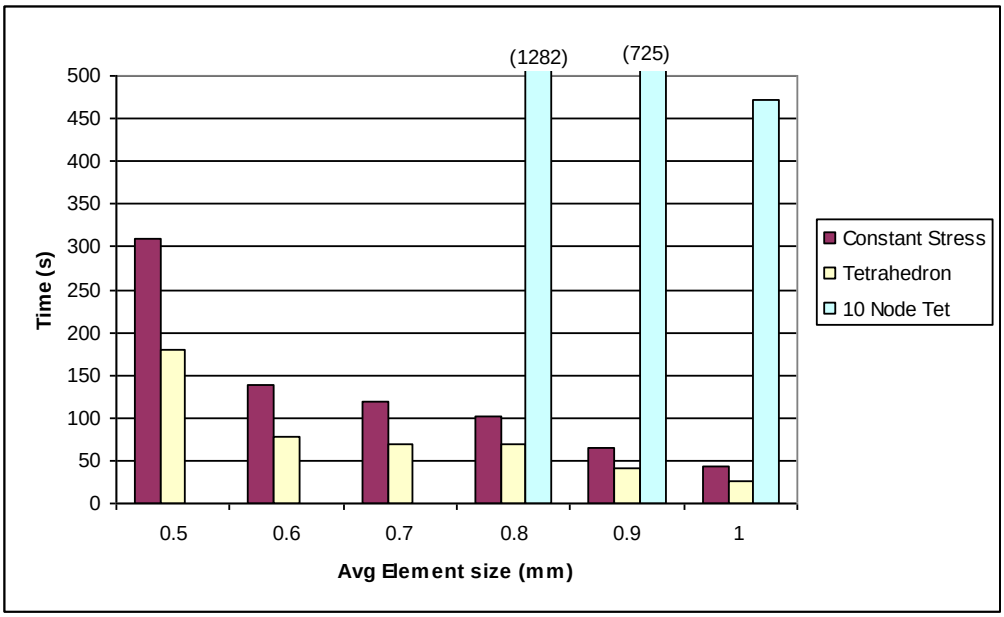
Parameters held constant: Material properties (all cortical), muscle load only

Parameter varied: Element size and element type

Results: The results are shown in SPECIFIC AIM 2: Figure 16. The constant stress elements are stiff in bending, the results from these elements are significantly higher than the other two element types tested. The quadratic (10 node) element results are about 1% larger than the 4 node tetrahedral elements, however, as shown in SPECIFIC AIM 2: Figure 17, the time to run the model is much larger using the quadratic tetrahedral elements, so the 4 node tetrahedral element with 1 integration point will be used in subsequent analyses. There is approximately a 2% change between the 0.5mm and 0.6mm element sizes, but about a 50% reduction in time using the 0.6mm elements. The smallest features in the model are the 2mm proximal exit holes in the docking technique. Using the 0.6mm elements, the exit holes have 14 element edges representing the circumference. The 0.6mm element size with the 4 node tetrahedrals will be used in subsequent analyses.



SPECIFIC AIM 2: Figure 16 - Maximum Von Mises Stress Versus Element Size and Type



SPECIFIC AIM 2: Figure 17 - CPU time Vs Element Size and Element Type (Quad core computer, 8GB RAM)

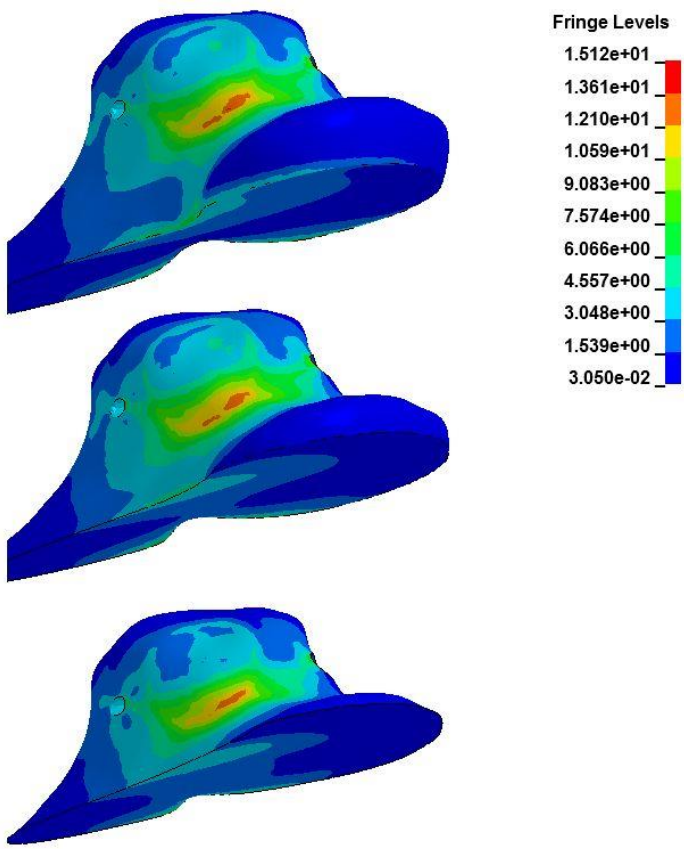
2) Effect of Varying Physical Cut Location

Description: In order to save computation time, it is desirable to keep the model of the medial epicondyle as small as possible. This study looked at the effect of changing the position where the model of the medial epicondyle was truncated on the maximum stress.

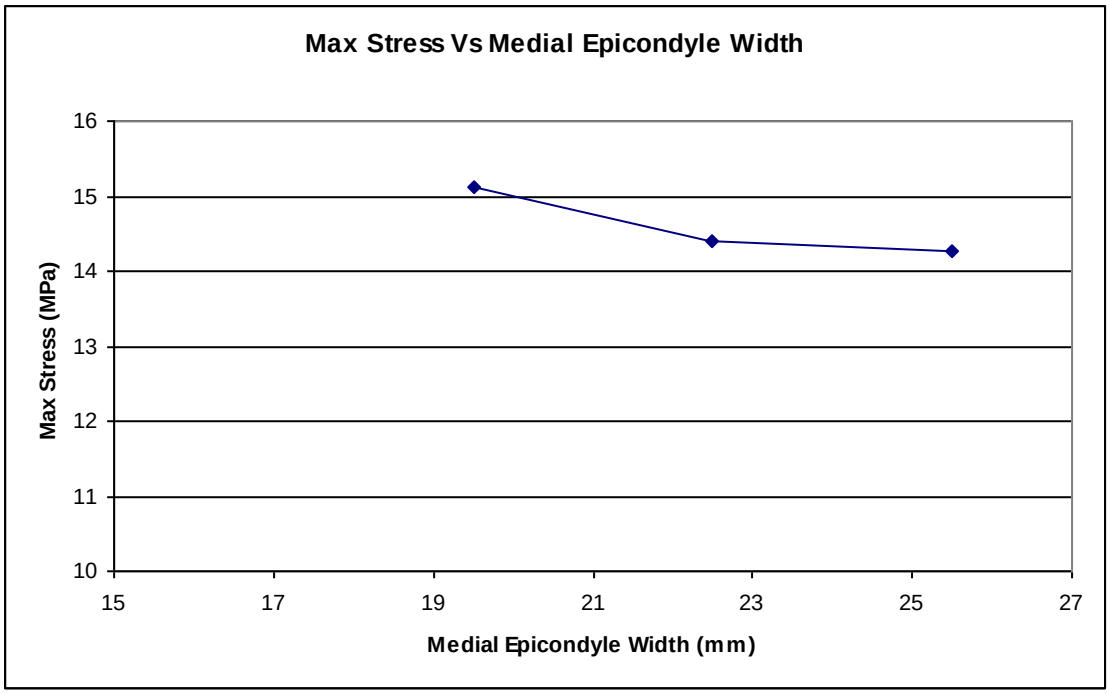
Parameters held constant: Material properties (all cortical), muscle load only

Parameter varied: Width of medial epicondyle (3 levels)

Results: The results are shown in SPECIFIC AIM 2: Figure 18 and SPECIFIC AIM 2: Figure 19. There was less than a 1% change when going from 22.5 mm to 25.5mm width, so the 22.5mm wide model was used in subsequent analyses.



SPECIFIC AIM 2: Figure 18 - Stress in medial epicondyle at different cut locations, width= 25.5mm (top), width=22.5 (middle), width=19.5 (bottom). Units of stress are MPa.



SPECIFIC AIM 2: Figure 19 - Maximum stress versus width of medial epicondyle model

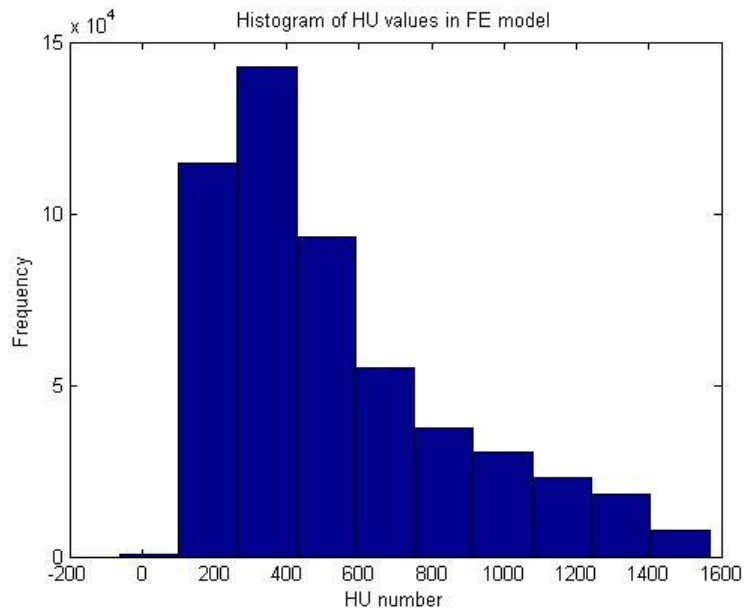
3) Effect of Varying Amount of Cortical and Cancellous Bone

Description: Each element of the FE model is assigned to be either cortical or cancellous bone, based on the position of the element centroid. The grayscale value of the CT voxel that the centroid lies in is used to categorize the element. A value of 500-600 HU has been used previously, based on visual inspection of the CT and the resulting material assignation. The purpose of this study is to determine how sensitive the bone stress is to the transition Hounsfield value.

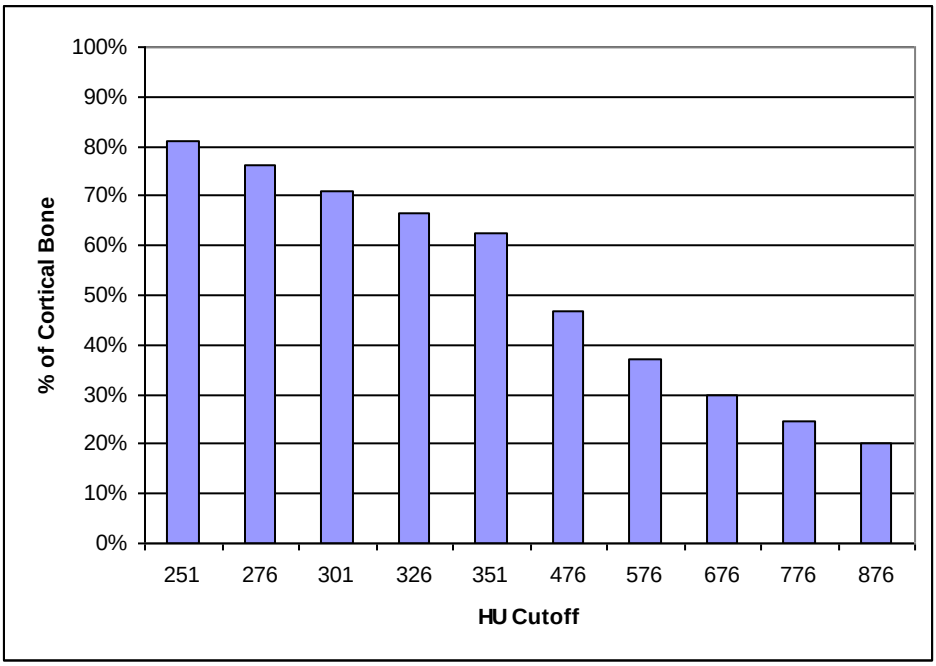
Parameters held constant: Muscle load, ligament load

Parameter varied: Transition value of Hounsfield unit to categorize element material

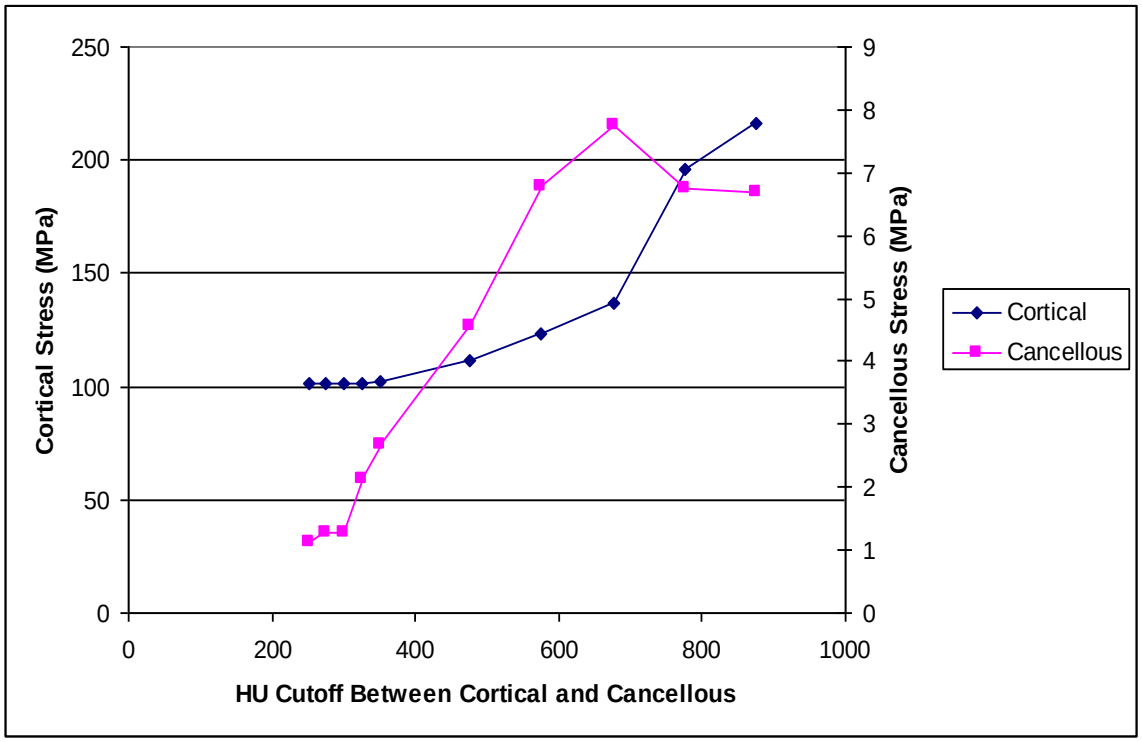
Results: As shown in SPECIFIC AIM 2: Figure 20, there is no clear division between cortical and cancellous bone. Depending on the transition value chosen, the total percentage of cortical bone changes appreciably. As shown in SPECIFIC AIM 2: Figure 21, over a realistic range of transition value from 400HU to 700HU the percentage of cortical bone elements changes by 30%. Considering the stress in the bone, the resulting maximum stresses are very sensitive to the transition value in the range of interest, as shown in SPECIFIC AIM 2: Figure 22.



SPECIFIC AIM 2: Figure 20 - Histogram of element HU number



SPECIFIC AIM 2: Figure 21 –Percentage of elements classified as cortical bone versus transition HU number



SPECIFIC AIM 2: Figure 22 - Maximum stress versus transition HU number

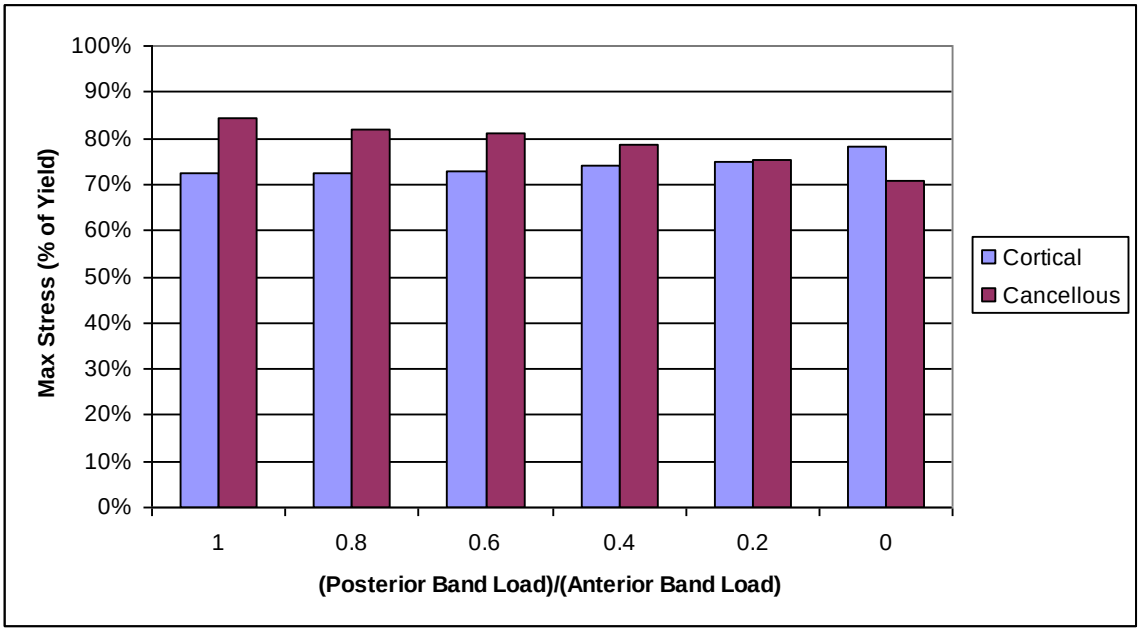
4) Effect of Varying Load on Anterior and Posterior Ligament Bands

Description: In the native ligament, the anterior band of the anterior bundle of the mUCL is taut in extension while the posterior band is taut in flexion. In the reconstructed ligament, the angular separation between the two bands in greater than in the native ligament. It is unclear how valgus load is shared by the two bands in the reconstructed ligament. In this parameter study, the ratio of the poster band load to the anterior band load is varied to determine how this changes the stress in the bone.

Parameters held constant: Muscle load

Parameter varied: Ratio of ligament load from 1 (equal load in both bands) to 0 (all valgus load resisted by the anterior band)

Results: The results of this study are shown in SPECIFIC AIM 2: Figure 23. When the ligament loads are equal (ratio=1) the cancellous loads are the greatest. When the anterior band alone resists the valgus load the cortical bone stress is the greatest. Overall, the magnitude of the change is relative small (6% change in the cortical stress, 12% change in the cancellous stress). In the subsequent studies the loads in both bands will be equal.



SPECIFIC AIM 2: Figure 23 - Maximum Stress Versus Ratio of Band Load

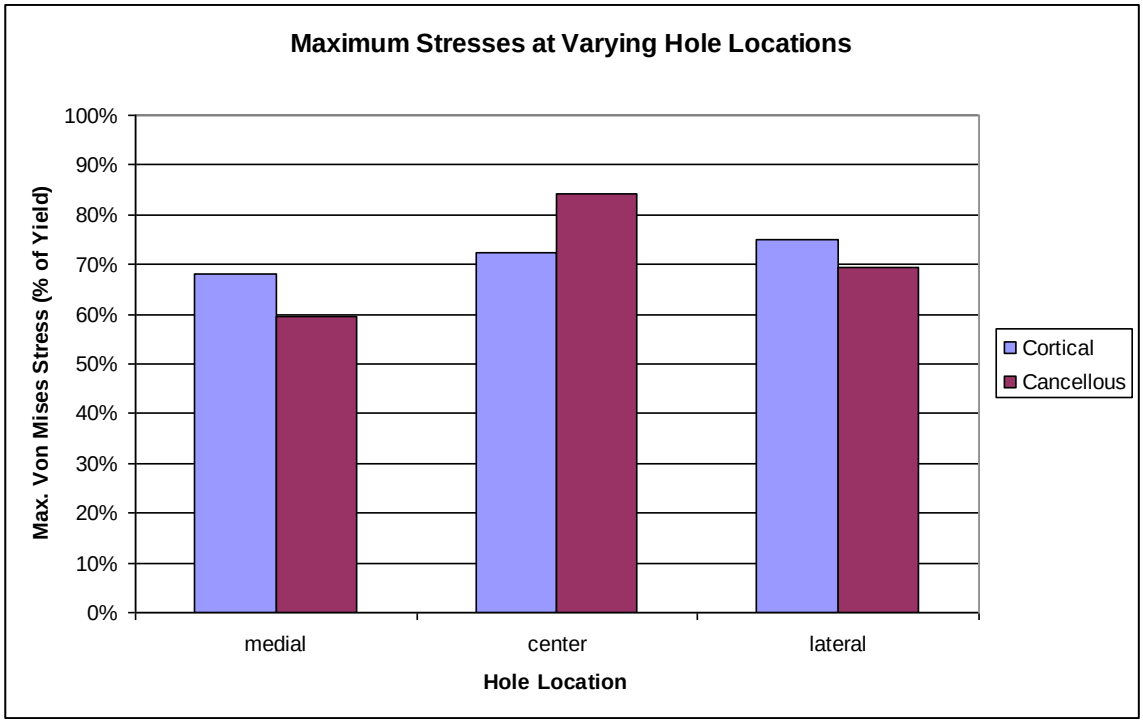
5) Effect of Varying Hole Position in Docking Reconstruction

Description: The effect of varying the location of the distal hole in the reconstruction is studied. The center location is located at the center of the native ligament, and the medial and lateral locations are offset 2mm from center in the respective directions.

Parameters held constant: Muscle load

Parameter varied: Hole location (3 levels)

Results: The results for the model simulating the docking technique are shown in SPECIFIC AIM 2: Figure 24. The cortical stress increases slightly as the hole position is moved from medial to lateral. The stress is greatest in the cancellous bone in the center position. The results of this model are different from the initial model in that there is not a localized stress concentration at the base of the medial epicondyle, due to the different morphology of the two different specimens.



SPECIFIC AIM 2: Figure 24 - Maximum bone stresses in the docking procedure model varying hole locations

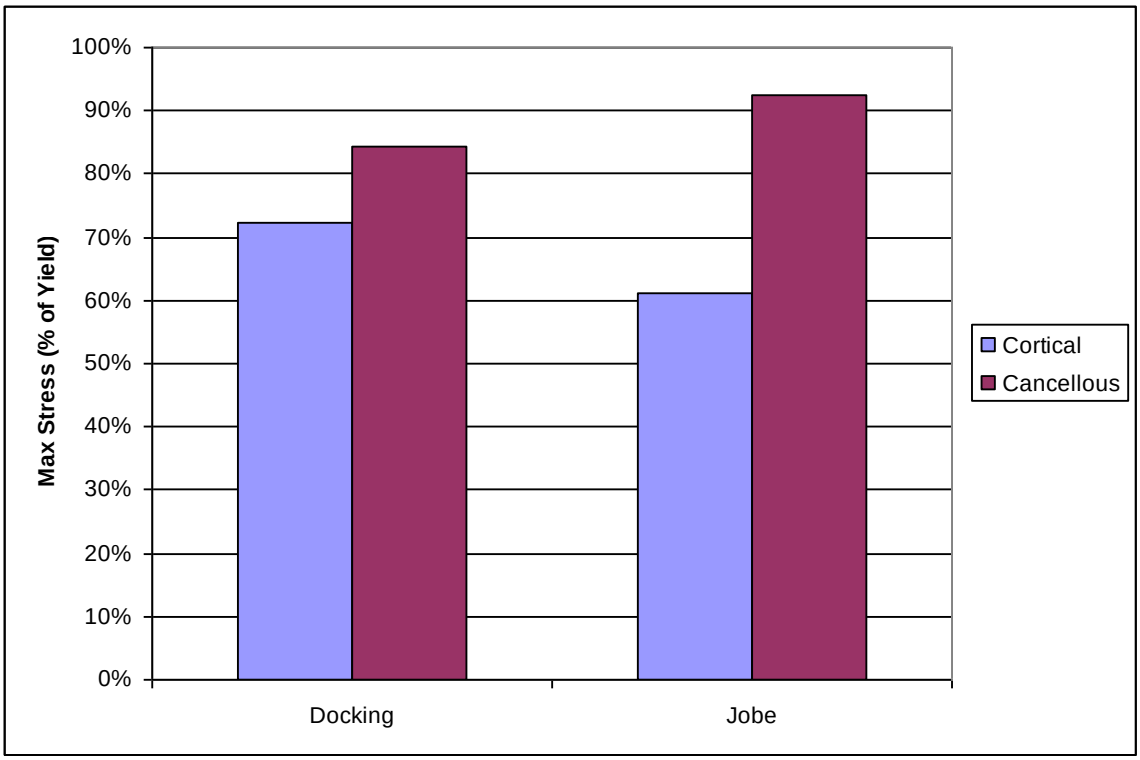
6) Effect of Varying Surgical Technique – Docking Vs. Modified Jobe

Description: The docking reconstruction procedure is compared to the modified Jobe reconstruction procedure. The main differences between the two techniques is the size of two converging proximal holes (2mm in the docking procedure, 3.2mm in the modified Jobe procedure) and the size and depth of the distal entry hole (4mm diameter in the docking procedure, 4.5mm diameter in the modified Jobe procedure).

Parameters held constant: Muscle load, distal entry hole (centered)

Parameter varied: Operative technique

Results: The results are shown in SPECIFIC AIM 2: Figure 25. Although the cortical stress is lower in the Jobe technique, the cancellous stress is greater.



SPECIFIC AIM 2: Figure 25 - Maximum bone stress comparing the docking technique to the modified Jobe technique

DISCUSSION: SPECIFIC AIM 2

The initial results of the humeral model clearly indicate that the placement of the insertion of the repair changes the stress distribution. Based solely on a stress-base criterion, the centralized hole placement is preferential because this location produced the lowest stresses. The maximum values of stress are well below the yield stress, as expected, given that mUCL reconstructions are

commonly performed with good outcomes. These results indicate that failures after reconstruction may be due to fatigue of the bone rather than a single overload during the recovery period. In the clinical study by Schwartz, the reconstructed mUCL remained intact, which indicates the failure load of the bone was lower than that of the reconstructed ligament. The clinical study also showed that the distal entry to the tunnel was involved in all of the cases, and the avulsed fragments did not include the proximal entry holes.

In the ulnar model, the higher stresses occur with the narrowest bone bridge, and the stresses decrease as the tunnel separation is increased, as was expected. Considering the strength of the bone bridge alone would lead to the conclusion that the largest distance between the tunnels is preferred, however two other factors should be considered. First, the proximity of the posterior tunnel to the ulnar nerve may restrict the placement of the more posterior hole. Second, the angle between the bands of the reconstructed tendon is large and does not replicate the native anatomic attachment of the ligament. Thus, the constraint of the reconstruction to valgus loading also may differ from the native case. Considering these factors, the best placement of the tunnels would be the smallest separation that allows for sufficient bone bridge strength. These preliminary results show that cortical bone stress remains less than the yield stress down to the smallest separation simulated (7.6mm).

The refined humeral model showed that the results are very sensitive to how the element materials are assigned. Future work should consider more sophisticated methods of determining the transition number, by using calibration artifacts in the CT scans to determine the density more accurately. Multiple levels of cancellous bone with different material properties may be necessary to accurately model the bones. This model also showed that the stresses are less sensitive to how the load is distributed between the two bands of the reconstructed ligaments. The initial model simulated the modified Jobe technique, and the hole position study in the refined model simulated the docking technique. Even though the techniques were different, the position of the entry hole showed similar results, in that cortical stress was not very sensitive to hole position (less than 10% change across hole positions in both models) and the cancellous stress was more sensitive to hole position (10% or greater change in both models). The refined model differed from the initial model in that there is not a localized stress concentration at the base of the medial epicondyle, due to the different morphology of the two different specimens used to create the models. Finally, this model shows that the docking technique does not display lower stresses in the cortical bone, despite the smaller drill sizes used to create the tunnels.

PRESENTATIONS and ABSTRACTS

An abstract including the initial results of the humeral model was accepted to the annual meeting of the Orthopedic Research Society and was presented at a poster session. An abstract including the results of the ulnar model was delivered as a podium presentation at the Summer Bioengineering Conference of the ASME and the use of strain to find the optimal angle at which to perform surgery was presented as a poster at that same meeting. The use of the physiologic elbow simulator with an example from ligament strains was included as a poster at the Biomedical Engineering Society meeting.

Miller, MC; Cook, HA; Akhavan, S; DeMeo, P J; “Finite Element Analysis of the Ulnar Tunnel in Ulnar Collateral Ligament Reconstruction”, American Society of Mechanical Engineers

Bioengineering Division Annual Meeting, 2010.

Mohaghegh Motlagh, A;. Cook, HA, Kim, S; DeMeo, PJ; Akhavan, S; Miller, MC; "The strain in the medial ulnar collateral ligament is localized in both the anterior and posterior bands of the anterior bundle" American Society of Mechanical Engineers Bioengineering Division Annual Meeting, 2010.

Miller, MC; Cook, HA; DeMeo, P J; "Computational Study of the Stress in the Medial Epicondyle Before and after UCL Reconstruction", Transactions of the Orthopaedic Research Society", 2010.

Schimoler, PJ; Kuxhaus, L; Vipperman, JS; Miller, MC; "Robotic controller design for an elbow simulator" Biomedical Engineering Society 2009.

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

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 ☐Accepted ☐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:

The use of strain to find the optimal angle for elbow ligament surgery. The articles on the finite element analysis of hole placement will be submitted to the American Journal of Sports Medicine.

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.

None

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.

Patrick J DeMeo, MD: Dr. DeMeo is a practicing orthopaedic surgeon specializing in Sports Medicine. He serves as team physician for the Pittsburgh Pirates Major League Baseball team. Dr. DeMeo is interested in improving care for athletes and is especially interested in the problems experienced by baseball pitchers.

Mark Carl Miller, PhD: Dr. Miller directs the Orthopaedic Biomechanics Laboratory at Allegheny General Hospital. He also serves as an Associate Research Professor at the University of Pittsburgh where he directs the study of graduate students working on problems in orthopaedic surgery.

Harold A. Cook, MS: Mr. Cook is a research engineer who has 15 years of experience as a consultant to the industrial and medical communities. While performing work in finite element analysis and product development, he is finishing a doctoral degree in Mechanical Engineering.