Bioskills Labs for Research & Development:

Considerations for Working with Human Tissue in a Research Environment

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7th Annual Bioskills Laboratory Symposium
August 15, 16 2016

Disclosures

- I have no conflicts related to this talk.

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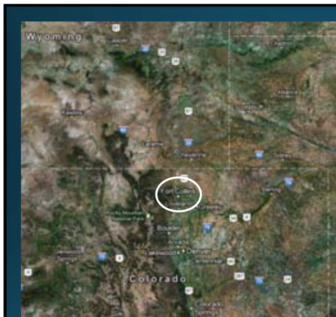

MS & PhD – Colorado State University

- Mechanical Engineering
- Thesis and Dissertation work in orthopaedic biomechanics

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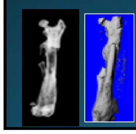
My Areas of Research Focus

Basic Science / Discovery
- Bone regeneration
- Protein delivery
- Biomaterials
- Fracture repair & healing
- Bone allograft science
- MEMS



Applied/Translational Biomechanics
- Medical device evaluation
- Medical device efficacy
- Benchtop to Bedside

Pre-Clinical Orthopaedic Biomechanics
- Tendon repair (Achilles, RCR)
- Biomaterial scaffolds
- Biologics

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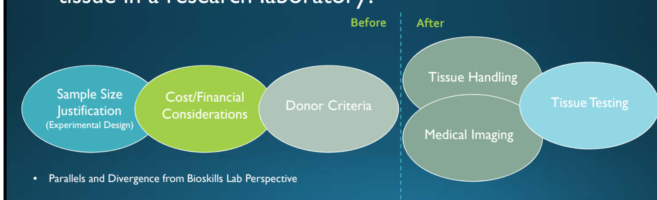
Human Tissue Use for Research Purposes

- What are unique considerations for handling human tissue in a research laboratory?



- Parallels and Divergence from Bioskills Lab Perspective

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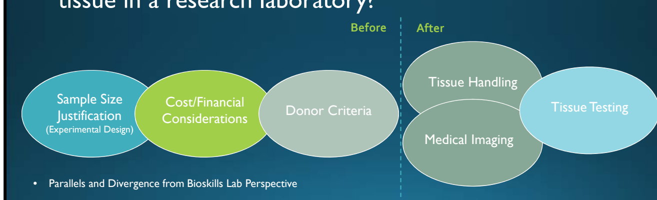
Human Tissue Use for Research Purposes

- What are unique considerations for handling human tissue in a research laboratory?



- Parallels and Divergence from Bioskills Lab Perspective

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Considerations PRIOR to Tissue Acquisition

Sample Size Justification (Experimental Design)

Cost/Financial Considerations

All great studies start with a great experimental design!!

- Studies we run are hypothesis- / question-driven:
  - Benchmark new technology
  - Prove superiority for clinical introduction
- Need to power (statistically) our studies to test the hypothesis / answer the research question:
  - Exhaustive literature search based on prior studies of similar scope
  - Understanding of inherent biomechanical variability {affected by bone quality}

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Considerations PRIOR to Tissue Acquisition

Sample Size Justification

Cost/Financial Considerations

All great studies start with a great experimental design!!

- Studies powered to avoid a Type II statistical error.

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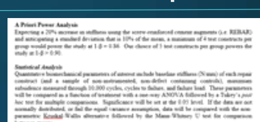
Considerations PRIOR to Tissue Acquisition

Sample Size Justification (Experimental Design)

Cost/Financial Considerations



A Priori Power Analysis
Expecting a 20% increase in stiffness using the screw-reinforced cement augments (i.e. REBAR) and anticipating a standard deviation that is 10% of the mean, a minimum of 4 test constructs per group would power the study at 1-β = 0.86. Our choice of 5 test constructs per group powers the study at 1-β > 0.90.

Statistical Analysis
Quantitative biomechanical parameters of interest include baseline stiffness (N/mm) of each repair construct (and a sample of non-instrumented, non-defect containing controls), maximum subsidence measured through 10,000 cycles, cycles to failure, and failure load. These parameters will be compared as a function of treatment with a one-way ANOVA followed by a Tukey's *post hoc* test for multiple comparisons. Significance will be set at the 0.05 level. If the data are not normally distributed, or fail the equal variance assumption, data will be compared with the non-parametric Kruskal Wallis alternative followed by the Mann-Whitney U test for comparison between groups.

- More tissue = better experiment BUT more tissue = more $$$$;
- Cost / benefit consideration – especially important to granting agencies;
- IF we can answer the research question with 12 specimens, NO need to test 24 specimens!

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Considerations PRIOR to Tissue Acquisition

Sample Size Justification (Experimental Design)

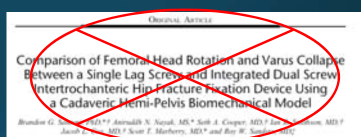
Cost/Financial Considerations

- We test a MINIMUM of 6 samples/specimens <u>per</u> treatment group;
- Difficult to justify otherwise and leads to peer-review scrutiny;

Considerations PRIOR to Tissue Acquisition

Sample Size Justification (Experimental Design)

Cost/Financial Considerations


Original Article

~~Comparison of Femoral Head Rotation and Varus Collapse Between a Single Lag Screw and Integrated Dual Screw Intertrochanteric Hip Fracture Fixation Device Using a Cadaveric Hemi-Pelvis Biomechanical Model~~

- Time-intensive consideration that may happen months prior to tissue acquisition.
- If done **inappropriately,** can lead to rejection [waste of time, resources, tissue, $$]

Considerations PRIOR to Tissue Acquisition

Donor Criteria

- Determined during experiment planning discussions w/ physicians.

Who is affected most by this particular orthopedic injury/problem?

Study findings most applicable to clinical reality

Considerations PRIOR to Tissue Acquisition

Donor Criteria → AGE

Example #1: Fixation of Vertical Femoral Neck Shear Fractures

- Occurs in younger patients (traumatic injury)
- Good bone stock

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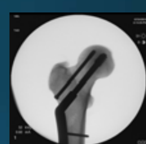
Considerations PRIOR to Tissue Acquisition

Donor Criteria → AGE



Example #1: Fixation of Vertical Femoral Neck Shear Fractures

- Donor age range: 29 – 54 yrs.

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Considerations PRIOR to Tissue Acquisition

Donor Criteria → AGE

Example #2: Fixation of Supracondylar Distal Femur Fractures

- Occurs in geriatric patients (traumatic injury)
- Compromised/poor bone quality

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Considerations PRIOR to Tissue Acquisition

Donor Criteria → AGE

Example #2: Fixation of Supracondylar Distal Femur Fractures

- Donor age range: 71 – 90 yrs.

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Considerations PRIOR to Tissue Acquisition

Donor Criteria → GENDER

Example: Fixation of Intertrochanteric Femur Fractures

- Occurs in older patients
- Primarily in females >65 with compromised bone quality

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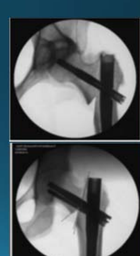
Considerations PRIOR to Tissue Acquisition

Donor Criteria → GENDER

Example: Fixation of Intertrochanteric Femur Fractures

- Donor criteria: all females, age range: 68 – 79 yrs.
- Average T-score: -1.6, osteopenia



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Considerations AFTER Tissue Acquisition

Tissue Handling

- Follow written SOPs in the lab
- Govern good tissue handling practices from safety perspective

MOST IMPORTANT CONSIDERATION FOR RESEARCH PURPOSES

- Handle the tissue in such a way that it's inherent biomechanical properties are not altered;
- GOAL: tissue behavior during testing is as close as possible to in vivo behavior.

Considerations AFTER Tissue Acquisition

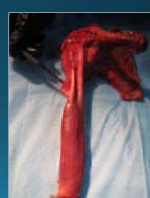
Tissue Handling

HOW DO WE ACCOMPLISH THIS?

(1) Minimize the # of freeze/thaw cycles

GOAL = 3

#1 Bulk Tissue Dissection



Considerations AFTER Tissue Acquisition

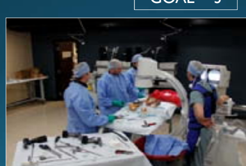
Tissue Handling

HOW DO WE ACCOMPLISH THIS?

(1) Minimize the # of freeze/thaw cycles

GOAL = 3

#2 Tissue Instrumentation



Considerations AFTER Tissue Acquisition

Tissue Handling

HOW DO WE ACCOMPLISH THIS?

(1) Minimize the # of freeze/thaw cycles

GOAL = 3

#3 Tissue Testing

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Considerations AFTER Tissue Acquisition

Tissue Handling

HOW DO WE ACCOMPLISH THIS?

(2) Keep the tissue hydrated at all times

Bulk Tissue Dissection

Tissue Instrumentation

Tissue Testing

Spray every 15 minutes w/ 0.9% NaCl

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Considerations AFTER Tissue Acquisition

Tissue Handling

HOW DO WE ACCOMPLISH THIS?

(3) Minimize tissue time in ambient

Typical test durations:

- minutes to 9 hours

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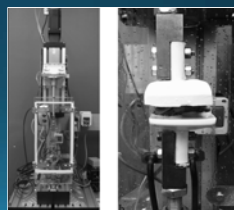
Considerations AFTER Tissue Acquisition

Tissue Handling

HOW DO WE ACCOMPLISH THIS?

(3) Minimize tissue time in ambient



Extreme test durations:

- 12+ hours

Considerations AFTER Tissue Acquisition

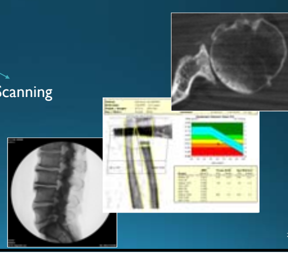
Medical Imaging

Nearly all of our studies have an imaging component to them.

CT Scanning

DEXA Scanning

Planar x-ray



Considerations AFTER Tissue Acquisition

Medical Imaging

Planar X-rays

Screening:

- Presence of implants;
- Prior fracture;
- Morphometric anomalies;
- Degree of degeneration (spine).

Considerations AFTER Tissue Acquisition

Medical Imaging

Planar X-rays

Confirm appropriate implant placement prior to testing

Considerations AFTER Tissue Acquisition

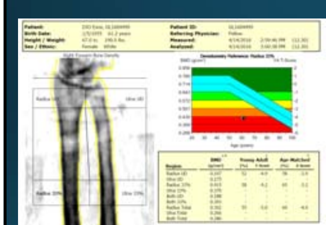
Medical Imaging

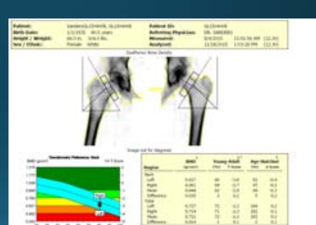
DEXA

Quantification of BMD & T-Score:

- Orthopaedic hardware behaves very differently depending on bone quality;
- Bone quality likely the greatest confounder in our research;
- Can use as a co-variate in statistical analysis.

Considerations AFTER Tissue Acquisition

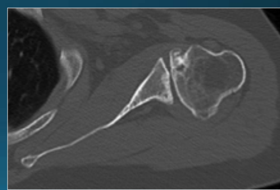




Considerations AFTER Tissue Acquisition

Medical Imaging

CT Scans



Purposes:

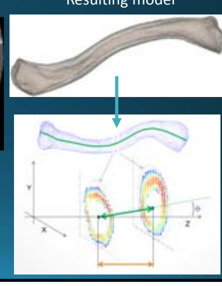
(1) Screening: pathologic lesions; glenoid morphometry
(2) 3D model development
  a. FE analyses
  b. 3D analysis

Considerations AFTER Tissue Acquisition

Clavicle

Canal

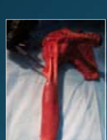
Resulting model



Considerations AFTER Tissue Acquisition

Tissue Testing

Maybe the MOST Challenging Consideration…
but it's also the most fun.



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Example Biomechanical Test Models 2010-Present

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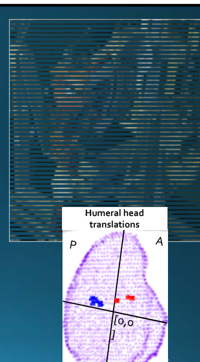
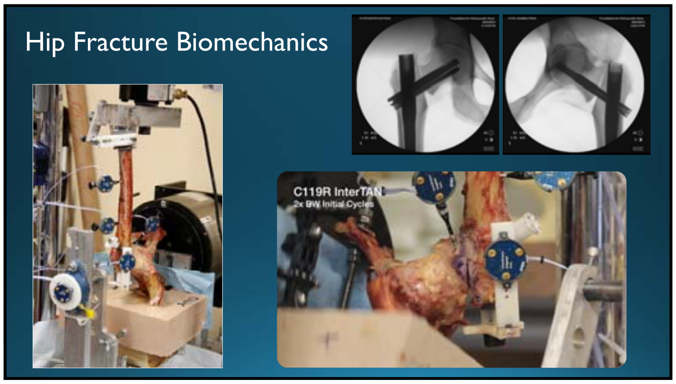
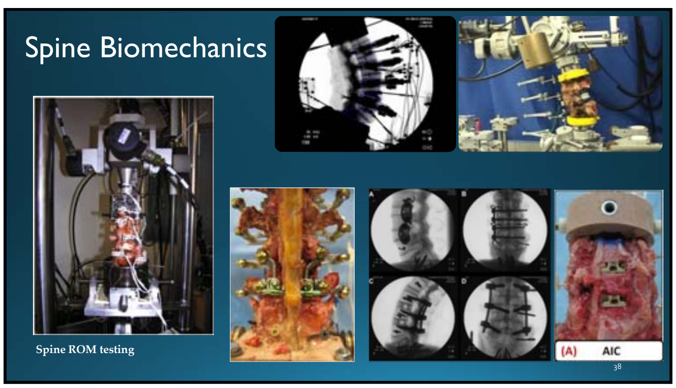
Shoulder Biomechanics




Hip Fracture Biomechanics
C119R InterTAN
2x BW Initial Cycles


Spine Biomechanics
Spine ROM testing
(A) AIC
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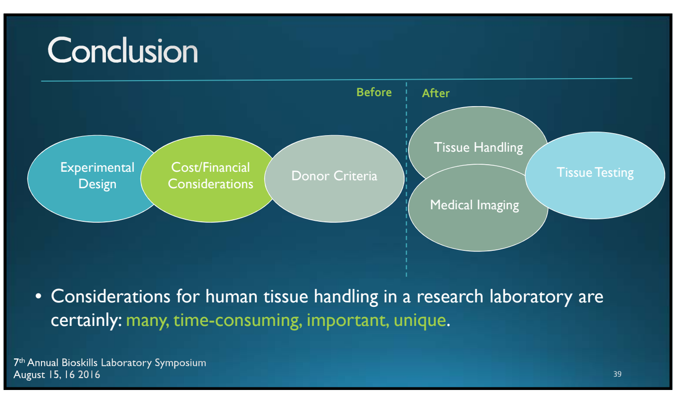
Conclusion
Before
After
Experimental Design
Cost/Financial Considerations
Donor Criteria
Tissue Handling
Medical Imaging
Tissue Testing
• Considerations for human tissue handling in a research laboratory are certainly: many, time-consuming, important, unique.
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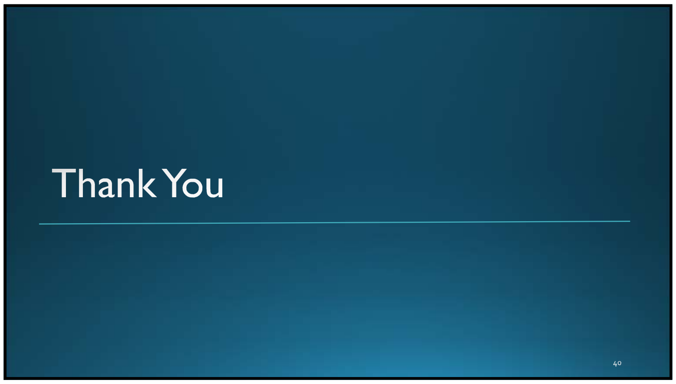
Thank You
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