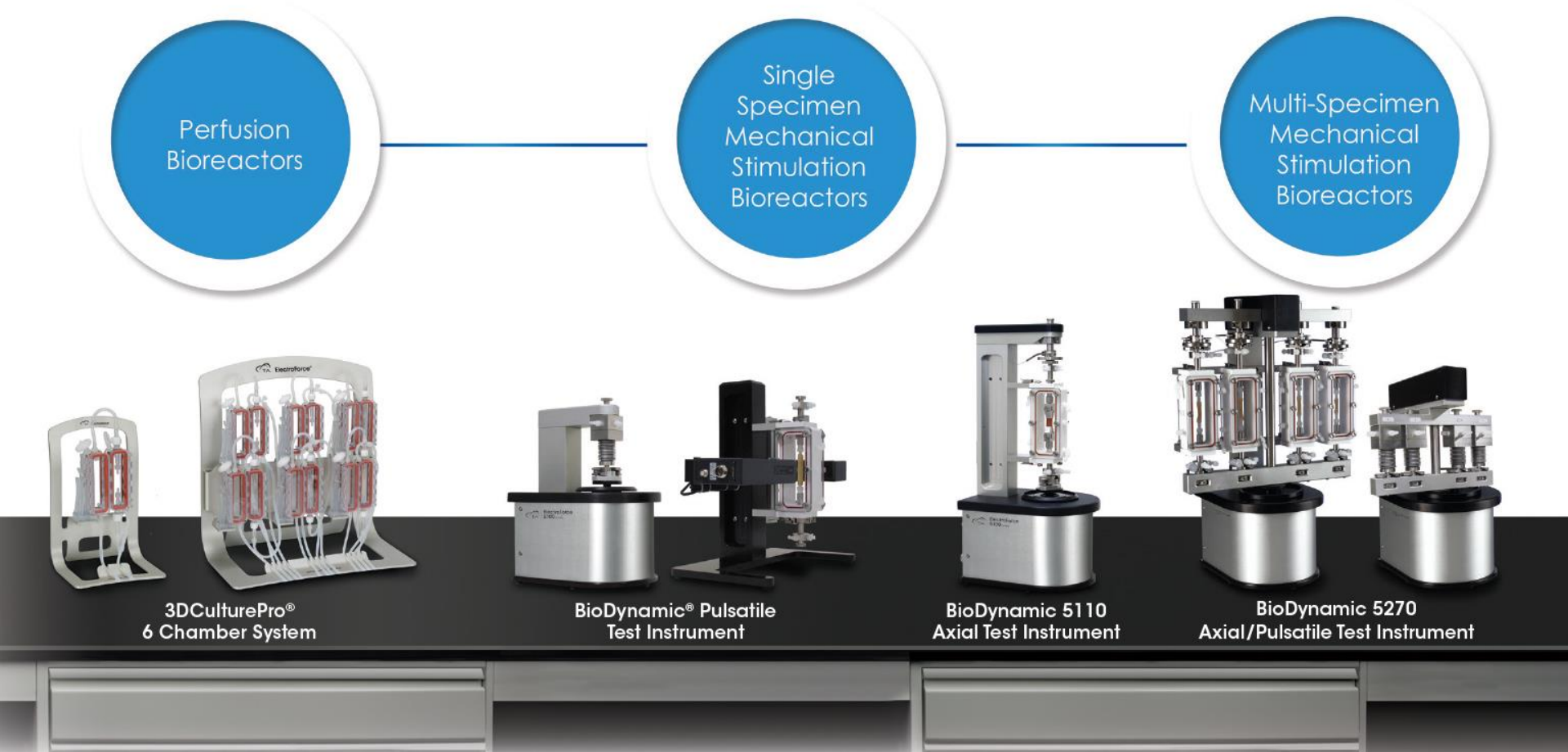
Mechanical Characterization and Stimulation Solutions for Biomaterials

BioDynamic Instruments



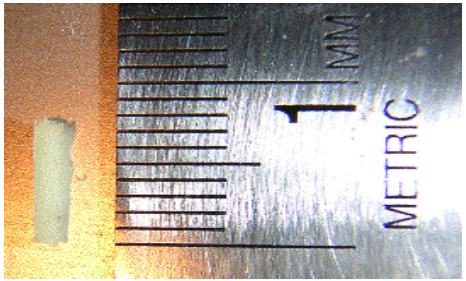
Biomaterials and Tissue Characterization

Application Examples

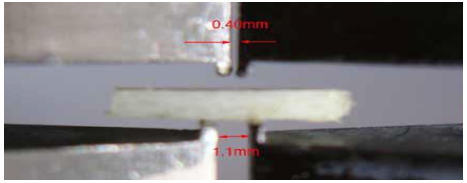
Bone Bending Creep Test

Clinical Need:
Understand how age impacts bone fragility

Research Need:
Testing of small bone specimens to examine age-related effects of collagen on the mechanical properties of bone



ElectroForce Application:
A 3200 with a standard system load cell and displacement sensor used to apply specific load levels to micro-machined human cortical bone and measure the corresponding displacement changes.

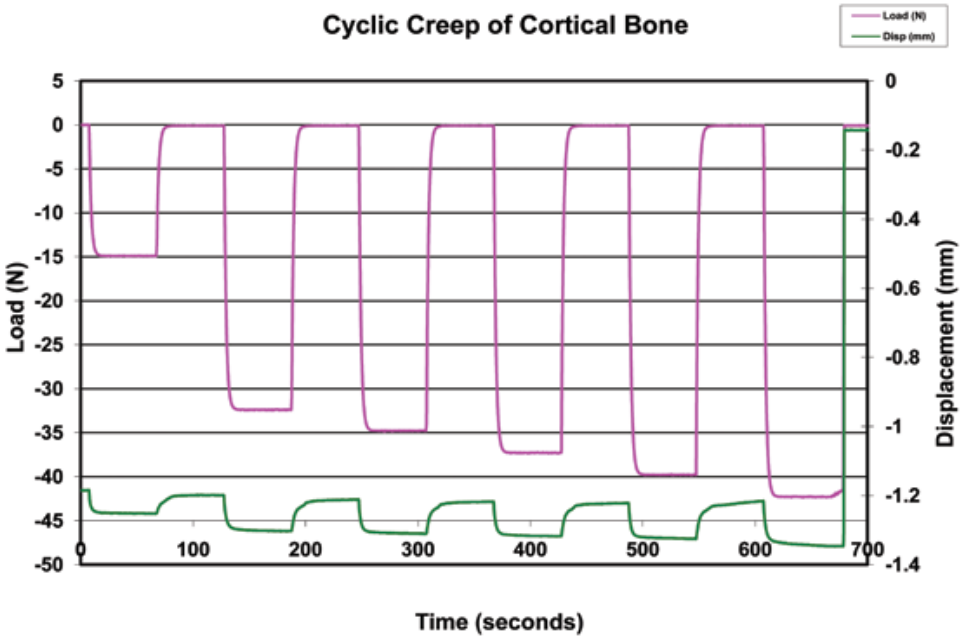


Bone Bending Creep Test

Parallelpiped Samples:
1mm x 1mm x 0.6mm

4 Point Bend Spacing:
0.4mm inner points
1.1mm outer points

Load levels:
35, 65, 70, 75, 80, and 85 MPa



Dental Biomaterials tests

Clinical Need:

Understand the impact of changes in dentin in an aging population

Research Need:

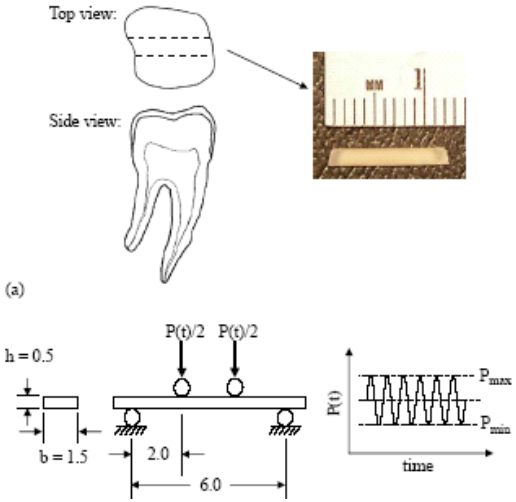
Characterize fatigue properties of dentin using two methods:

1) bending
2) crack growth

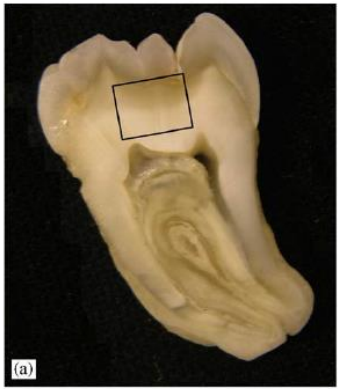
ElectroForce application:

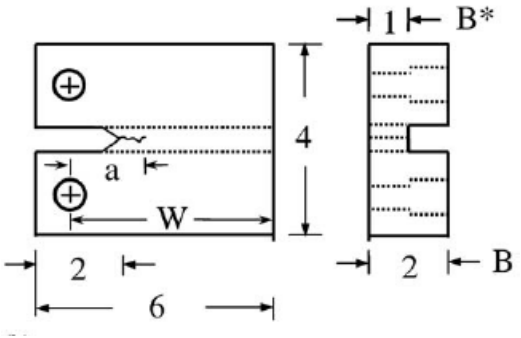
Using the ElectroForce 3200 to perform small amplitude fatigue tests on micro-samples of human dentin samples

4-Point Bending



Crack Growth





D. Arola et.al., "Effects of aging on the mechanical behavior of human dentin", Biomaterials 2004
DOI: 10.1016/j.biomaterials.2004.10.029

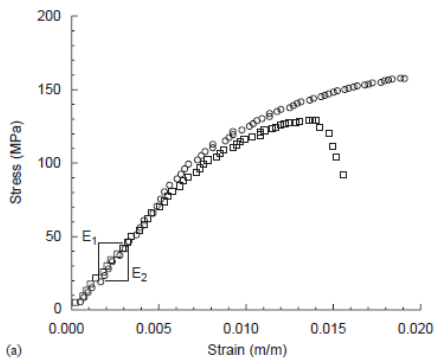
Dental Biomaterials tests

Results:

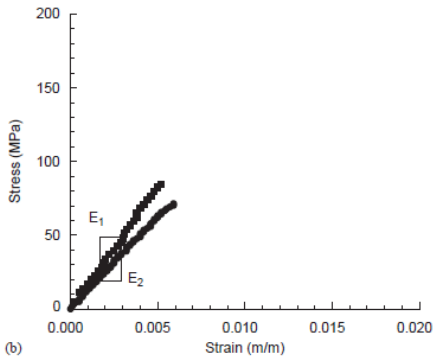
Stress-Strain plots show stronger and tougher results in young specimens

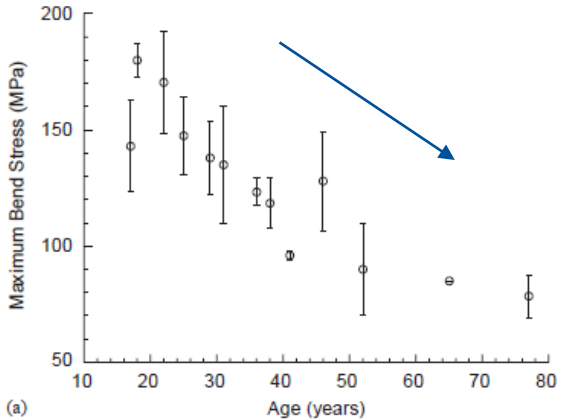
Clear trends in Max Stress and Energy

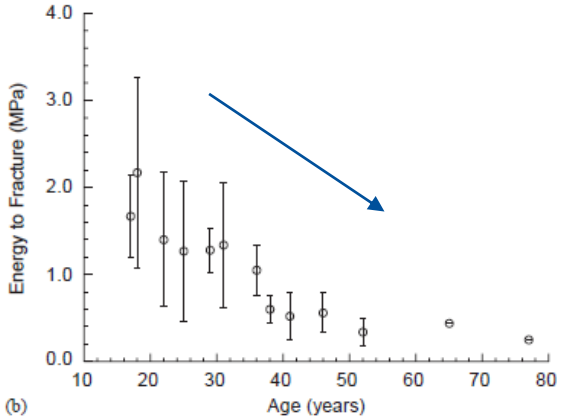
Young



Old







D. Arola et.al., “Effects of aging on the mechanical behavior of human dentin”, Biomaterials 2004
DOI: 10.1016/j.biomaterials.2004.10.029

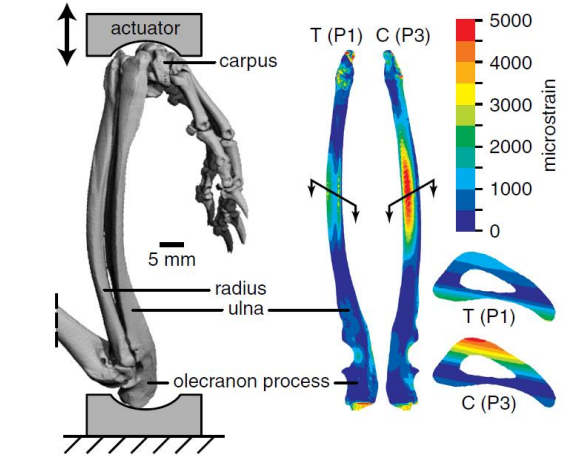
In Vivo Bone Loading

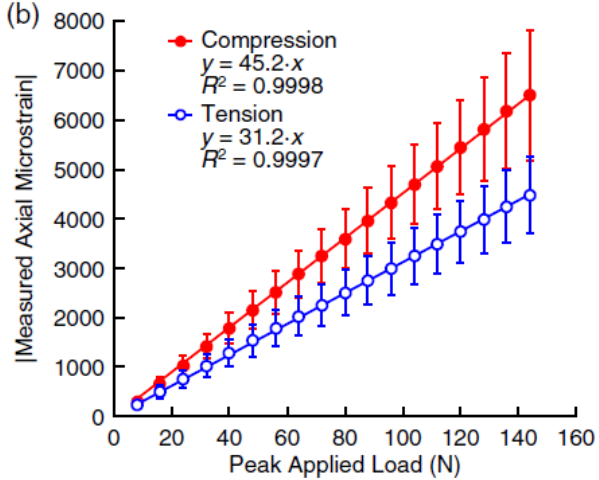
Clinical Need:
Better understanding of biochemical and biomechanical response of bone to mechanical loading

Research Need:
Develop and apply a model for in vivo bone loading that is quantifiable and reliable

ElectroForce Application (model calibration):
Compression loading of small animal ulna which creates quantifiable bending strains within bone

Calibrations were performed using strain gaged bones during axial loading with ElectroForce 3200 & 3300 instruments





A. Baumann et al., "Development of an in vivo rabbit ulnar loading model" *Bone 2015.* http://doi.org/10.1016/j.bone.2015.01.022

In Vivo Bone Loading

ElectroForce Application (In Vivo Loading):

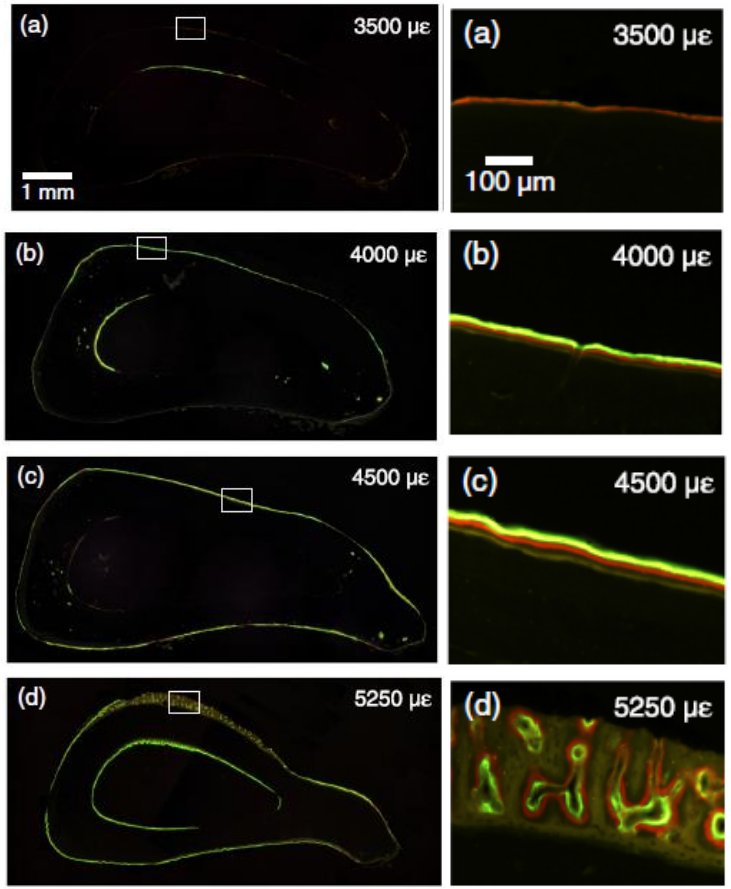
Cyclic 2Hz uniaxial compression for 360cycles/day with ElectroForce 3200

Multiple levels of peak compression strains from 3000 to 5250 microstrain (~60 to 125N applied loads)

InVivo Loading Results:

Periosteal bone formation was measured in response to different strain levels:

Control & <3000με	No measurable bone formation
3500με	Detectable but weak formation
4000 & 4500με	New lamellar bone
5250με	Significant woven bone formation



A. Baumann et al., "Development of an in vivo rabbit ulnar loading model" *Bone 2015.* http://doi.org/10.1016/j.bone.2015.01.022

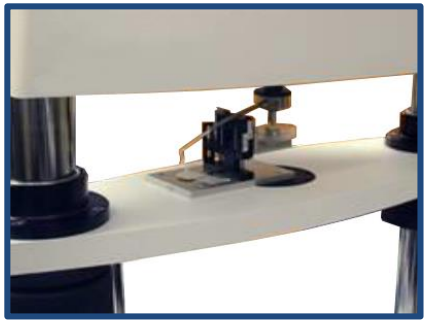
Cartilage Indentation

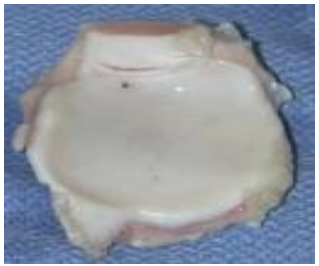
Clinical Need:
Determine mechanical properties of cartilage to better understand what will be needed for replacement material.

Research Need:
Understand the impact of indentation tip geometry and size on the results of indentation tests.

ElectroForce Application:
Determine Young's modulus utilizing an ElectroForce 3100 or 3200, indenters, and saline bath.

Bovine articular cartilage was compared to elastic foam and urethane rubber searching for suitable alternative for future studies.





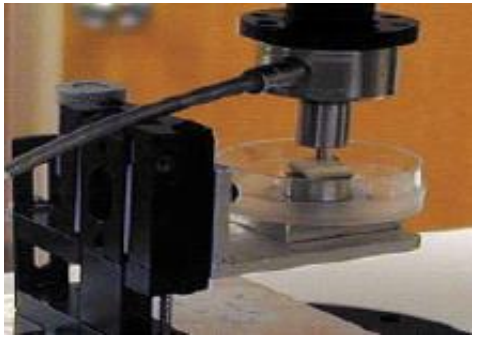
Ref: Application Brief: "[1]Characterizing Mechanical Properties of Cartilage in Situ App Brief", TA instruments

Cartilage Indentation

Testing Solution:

ElectroForce system used to conduct indentation test on urethane, foam and cartilage specimens:

- Preconditioned with cyclic indentation of -0.25/-0.125mm at 5 Hz for 20 cycles
- 40 minute recovery
- Indenter surface contact and then indent sample 0.15mm at 1.5 mm/sec rate
- 1200 sec displacement hold



Conclusion

- Data on urethane and foam compared favorably to cartilage and should prove useful in simulations

Ref: Application Brief: "[1]Characterizing Mechanical Properties of Cartilage in Situ App Brief", TA instruments

Hydrogels for Cartilage

Clinical Need:
Effective clinical treatments to repair cartilage (knee) injuries through tissue engineering

Research Need:
Determine the most appropriate scaffold material which mimics the physiological loading response of articular cartilage

ElectroForce Application:
Apply physiological loading profiles to characterize the mechanical response of hydrogels

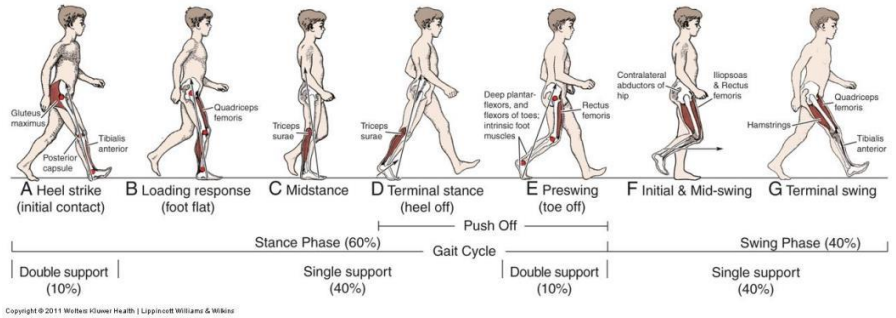
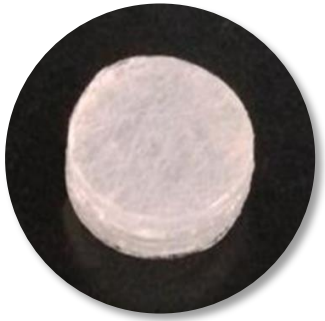


Image ref: Halonen et al., 2013

Hydrogels for Cartilage

- Samples punched from polyethylene glycol hydrogel sheets (Medline Ind.)
- Sample preloaded to 0.1 N
- Walking gait compression waveform was imported to WinTest

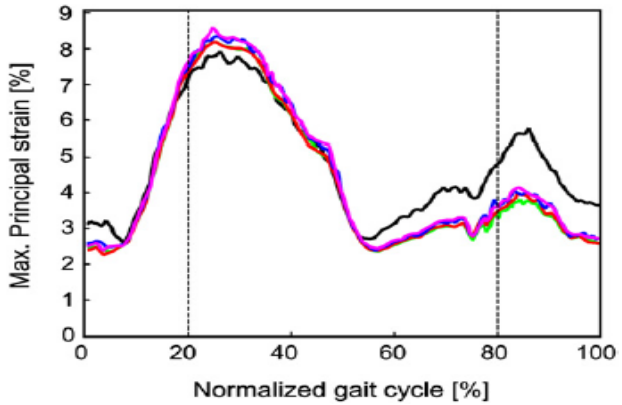


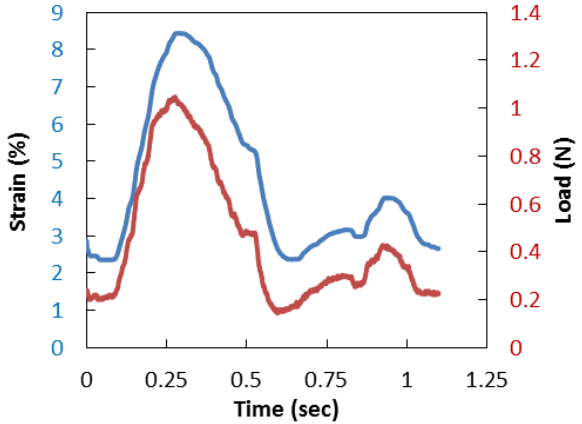
Ref: TA internal study

Hydrogels for Cartilage

Waveform of strain vs. gait cycle based on simulation of human walking

Walking speed of 5 km/h
Gait cycle of 1.1 sec





Ref: TA internal study

Hydrogels for Cartilage

ElectroForce 5500 Test Instrument with a multi-specimen fixture used to apply walking waveform compression on hydrogels

- Fixture used in combination with 24-well plate

Samples punched out of PEG hydrogel sheets

- 12 mm diameter, 1.2 mm height

Samples placed in saline-filled wells

ElectroForce 5500 Test Instrument with 24-Well Plate Fixture

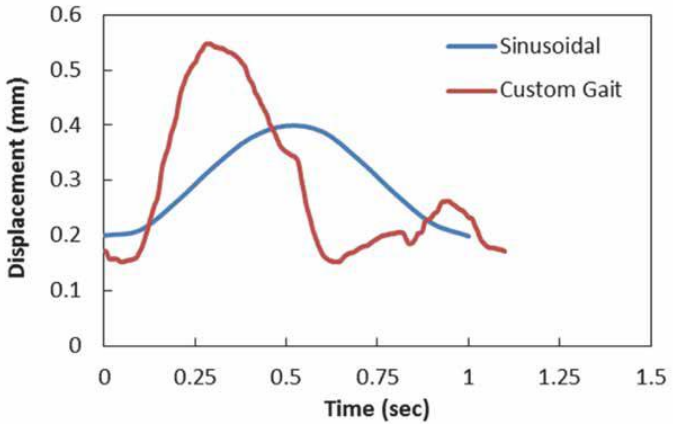
Ref: TA internal study

Hydrogels for Cartilage

Samples subjected to two loading waveforms:

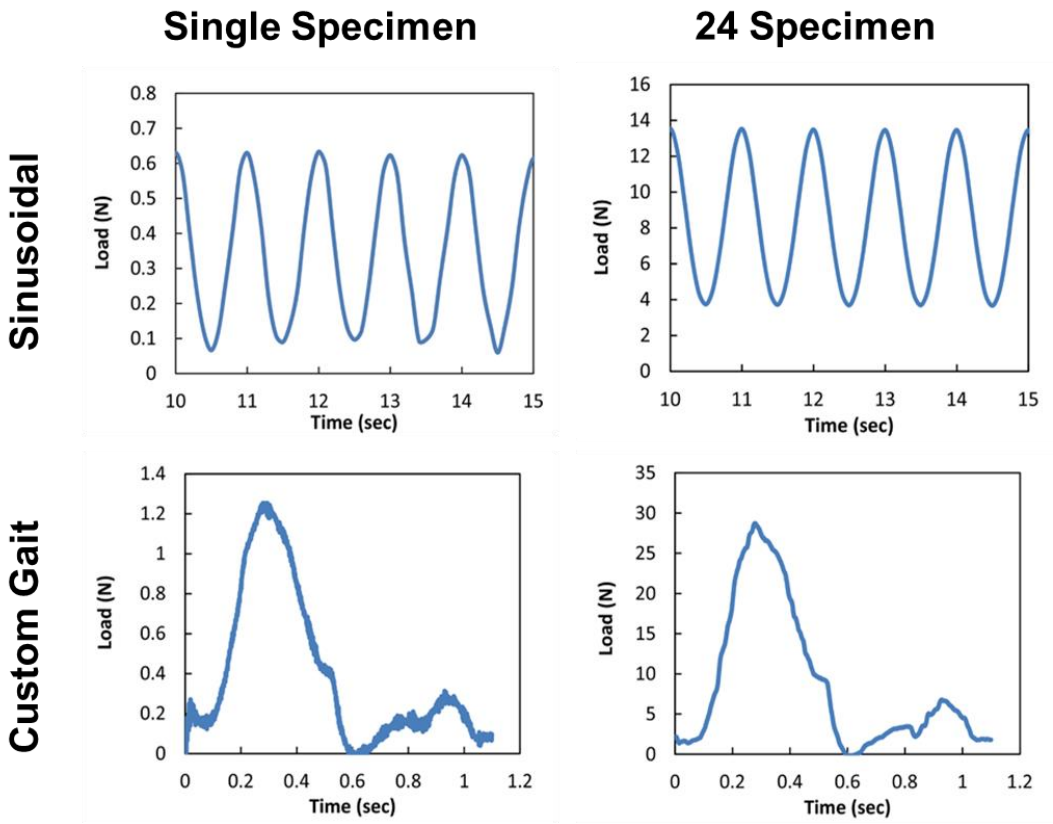
- *Sinusoidal*
- *Walking Gait (Custom)*

Experimental Conditions	
1 Specimen/Loaded	Sinusoidal & Custom Gait
24 Specimens/Loaded	Sinusoidal & Custom Gait
12 Specimens/Loaded & 12 Specimens/Unloaded	Custom Gait *3 samples each from loaded and unloaded groups tested to failure with single pair of platens



Ref: TA internal study

Hydrogels for Cartilage

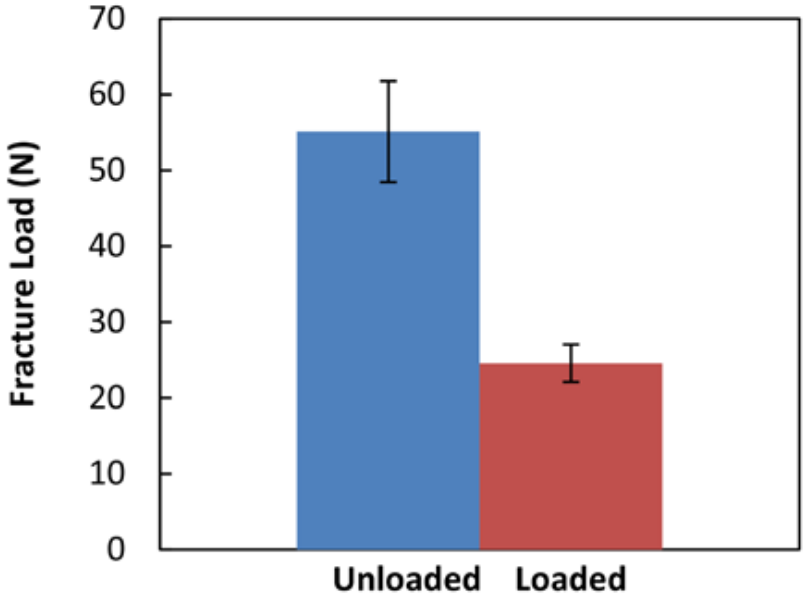


Ref: TA internal study

Hydrogels for Cartilage

Two sets of 24 samples were tested, to compare unloaded vs cyclically loaded specimen strength

Unloaded samples had a higher fracture load than loaded samples



Ref: TA internal study

5110 and 5210 Mechanical Simulation Bioreactors

Product Details

- Combining sterile biologic environment with mechanical stimulation and measurements
- Cell-culture incubator compatible
- One or four-chamber versions (5170 or 5270)
- Mechanical Forces up to 200 N
- 3 Fixture packages: Tubular, Strips and Disc
- Flexible, sterilizable chambers and flow-loops
- Peristaltic pump included: 0.1-280 mL/min

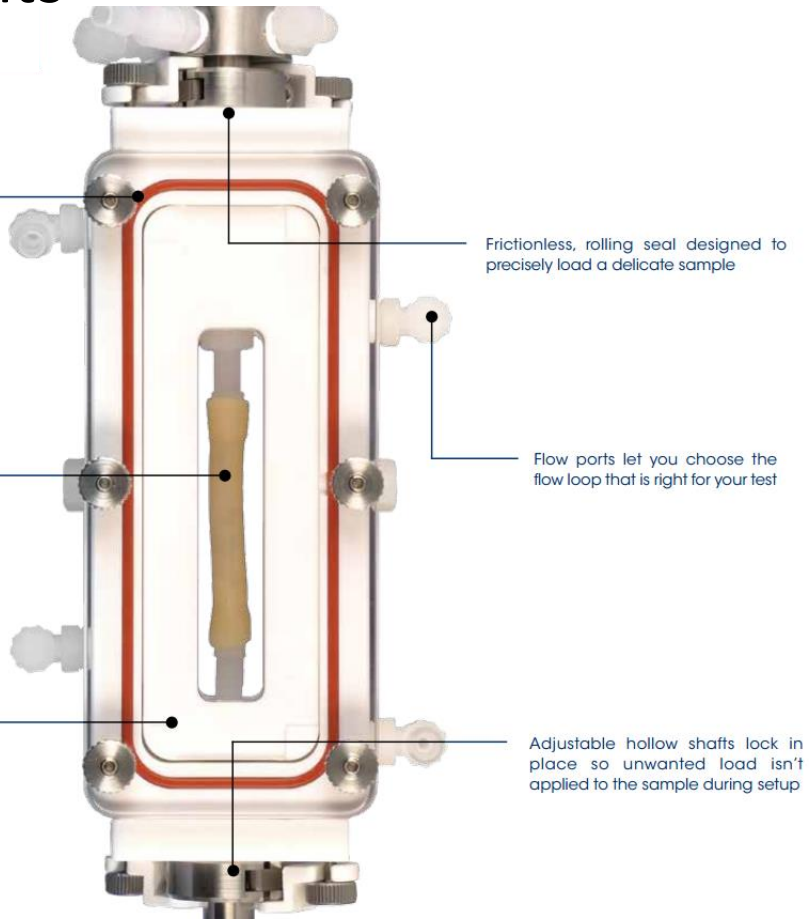
5170 and 5270 Mechanical Simulation Bioreactors

Product Details

- Combining sterile biologic environment with mechanical stimulation and measurements
- Cell-culture incubator compatible
- One or four-chamber versions (5170 or 5270)
- Mechanical Forces up to 200 N
- 3 Fixture packages: Tubular, Strips and Disc
- Flexible, sterilizable chambers and flow-loops
- Dynamic Pulsatile Pump assembly: Up to 8.8 mL/pulse plus 1760 mL/min mean flow

BioDynamic Instruments

Chamber Details



Degradation of PLGA

Clinical Need:
Determine the most appropriate biocompatible polymers which have different properties for different applications (tissue support or drug delivery)

Research Need:
Currently, biodegradation of scaffolds is assessed under static conditions, but the materials are subjected to a dynamic physiological environment once implanted

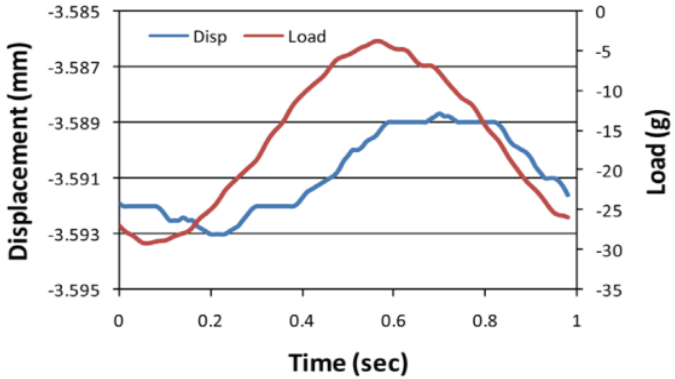
ElectroForce Application:
Investigate the degradation of a common biomaterial when subjected to long-term, dynamic loading

Ref: Application Brief: “Degradation of PLGA Scaffolds Under Dynamic Loading”, TA instruments

Degradation of PLGA

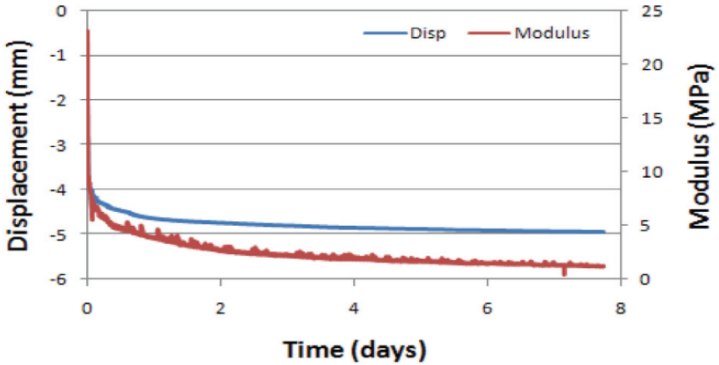
Test Groups:

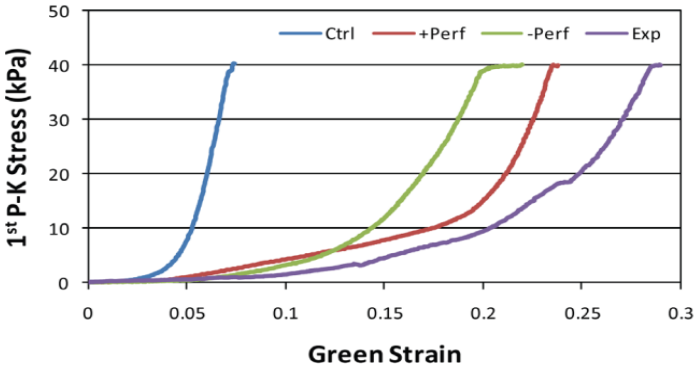
- *Dynamic*: sinusoidal compression (5 to 30 grams at 1 Hz) and static perfusion
- *+ Perfusion*: static perfusion only
- *- Perfusion*: stagnant saline (no perfusion)
- *Control*: completely dry



Ref: Application Brief: "Degradation of PLGA Scaffolds Under Dynamic Loading", TA instruments

Degradation of PLGA





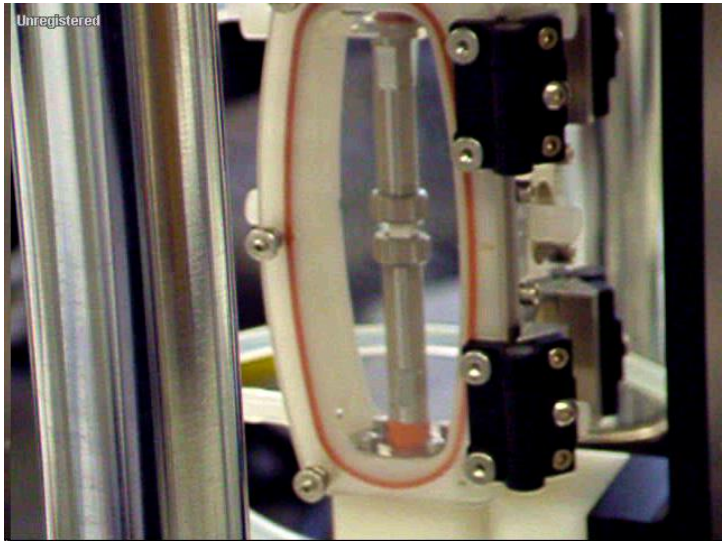
Ref: Application Brief: "Degradation of PLGA Scaffolds Under Dynamic Loading", TA instruments

Bone Tissue Engineering

Clinical Need:
Alternatives to chemical/drug treatment to stimulate bone formation

Research Need:
Stimulation differentiation and mineralized matrix production of hMSCs via compressive loading

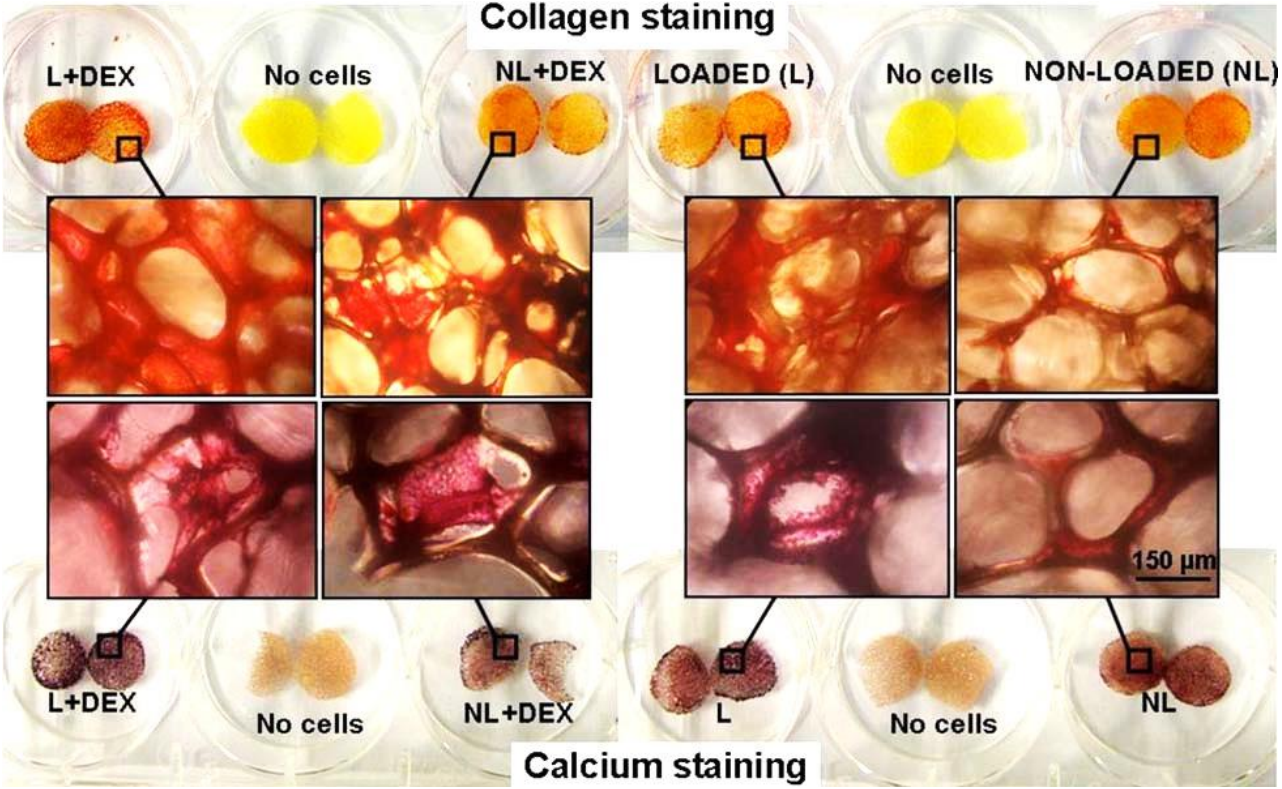
ElectroForce Application:
hMSC-seeded scaffolds (polyurethane) were periodically compressed (dynamic) using the 3200 Test Instrument with a BioDynamic chamber



Dr. Gwen Reilly's Group
University of Sheffield

K. Mallick et.al, "Three-dimensional porous bioscaffolds for bone tissue regeneration", Journal of Biomedical Materials Research 2012;
DOI: 10.1002/jbm.a.34238

Bone Tissue Engineering



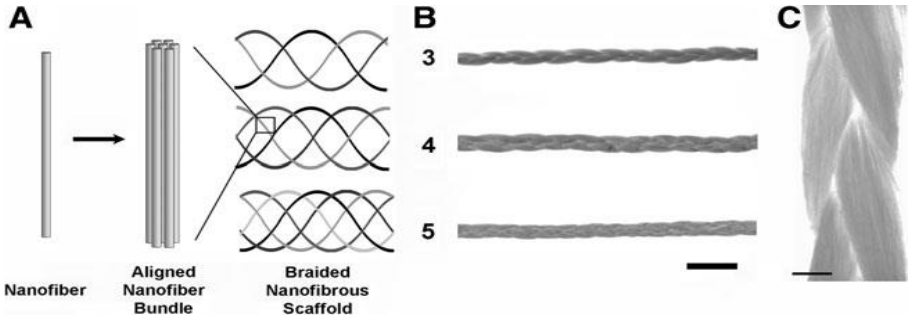
K. Mallick et.al, "Three-dimensional porous bioscaffolds for bone tissue regeneration", Journal of Biomedical Materials Research 2012;
DOI: 10.1002/jbm.a.34238

Tendon Tissue Engineering

Clinical Need: Develop alternative treatments and therapies for tendon repair

Research Need: Drive tenogenic differentiation of hMSCs cultured on scaffold made of braided electrospun poly(l-lactic acid) nanofibers.

ElectroForce Application: Use the 5210 BioDynamic Test System to (i) characterize and refine mechanical properties of scaffolds and (ii) direct stem cell differentiation with mechanical cues

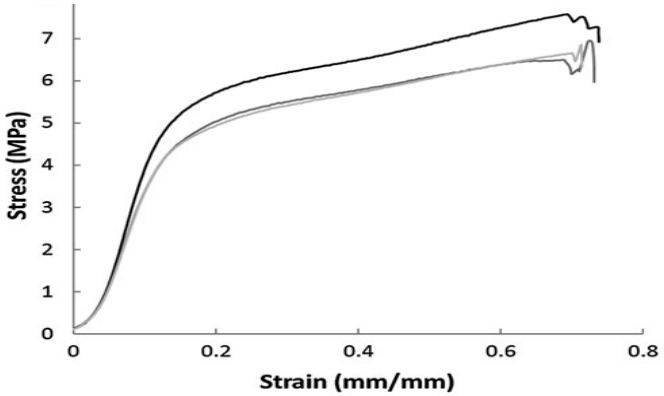


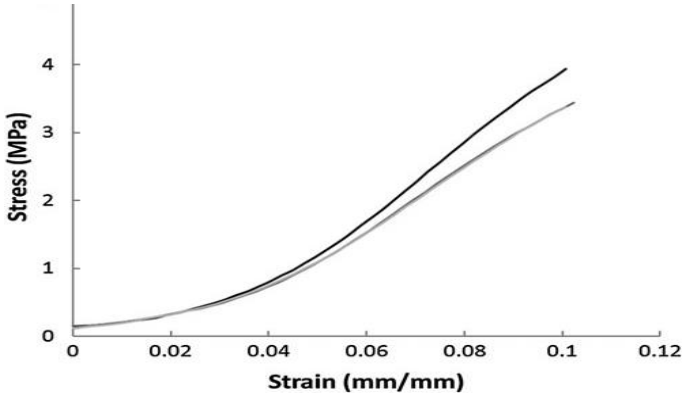
Dr. Wan-Ju Li's Laboratory
University of Wisconsin – Madison

[1]Stem Cell Differentiation App Brief

J. Barber, et.al., "Braided Nanofibrous Scaffold for Tendon and Ligament Tissue Engineering", Tissue Engineering: Part A; 2011
DOI: 10.1089/ten.tea.2010.0538

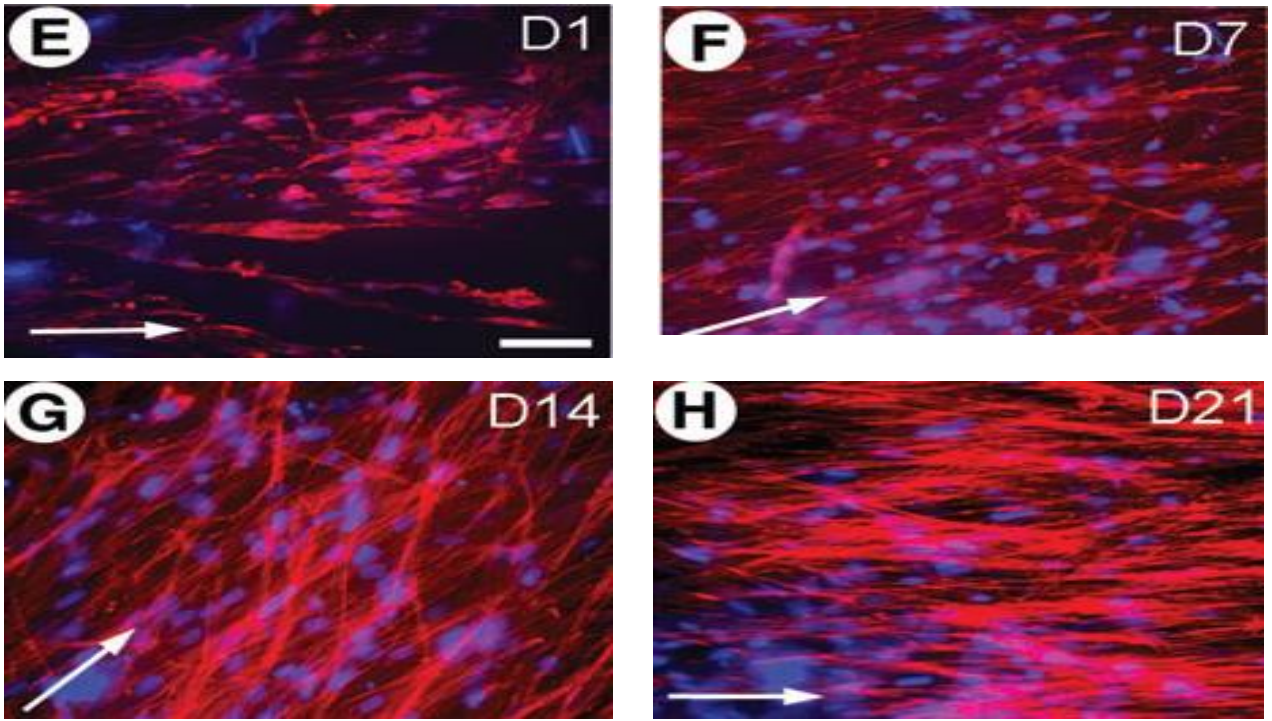
Tendon Tissue Engineering





J. Barber, et.al., “Braided Nanofibrous Scaffold for Tendon and Ligament Tissue Engineering”, Tissue Engineering: Part A; 2011
DOI: 10.1089/ten.tea.2010.0538

Tendon Tissue Engineering



J. Barber, et.al., “Braided Nanofibrous Scaffold for Tendon and Ligament Tissue Engineering”, Tissue Engineering: Part A; 2011
DOI: 10.1089/ten.tea.2010.0538

Airway Tissue Engineering

Clinical Need: Treatment for tracheal trauma or disease

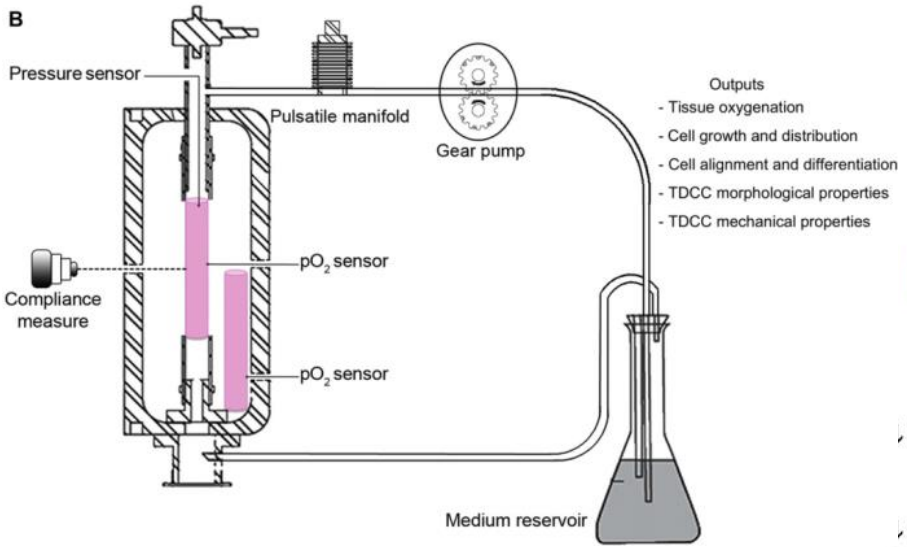
Research Need: Understand the effect of shear stress and circumferential strain on airway SMCs

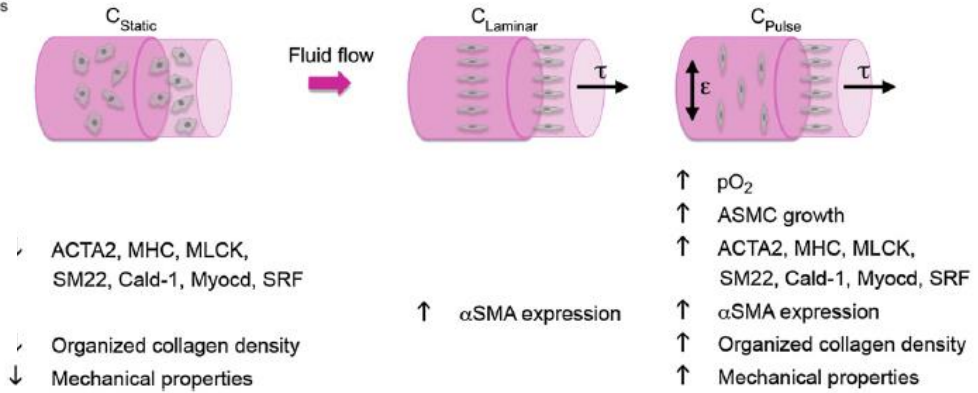
ElectroForce Application: Tissue engineered airway construct cultured under different mechanical conditions (Perfusion BioDynamic System). Circumferential strength measured after culture (3200 Test System)

Dr. Showan Nazhat's Laboratory
McGill University

C. Gheezi, et.al., "An airway smooth muscle cell niche under physiological pulsatile flow…", Biomaterials 2013
DOI: http://dx.doi.org/10.1016/j.biomaterials.2012.11.025

Airway Tissue Engineering





C. Gheezi, et.al., "An airway smooth muscle cell niche under physiological pulsatile flow…", Biomaterials 2013
DOI: http://dx.doi.org/10.1016/j.biomaterials.2012.11.025

THANK YOU