

The Effect of Menopause on Osteoporosis and Bone Degeneration In Mouse Models



Northeastern University
**Michael B. Silevitch and
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for STEM Education**

NSF #2150417



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SHEFELBINE LAB
MULTISCALE MECHANICS AND MUSCULOSKELETAL
MECHANOBIOLOGY (M⁴)



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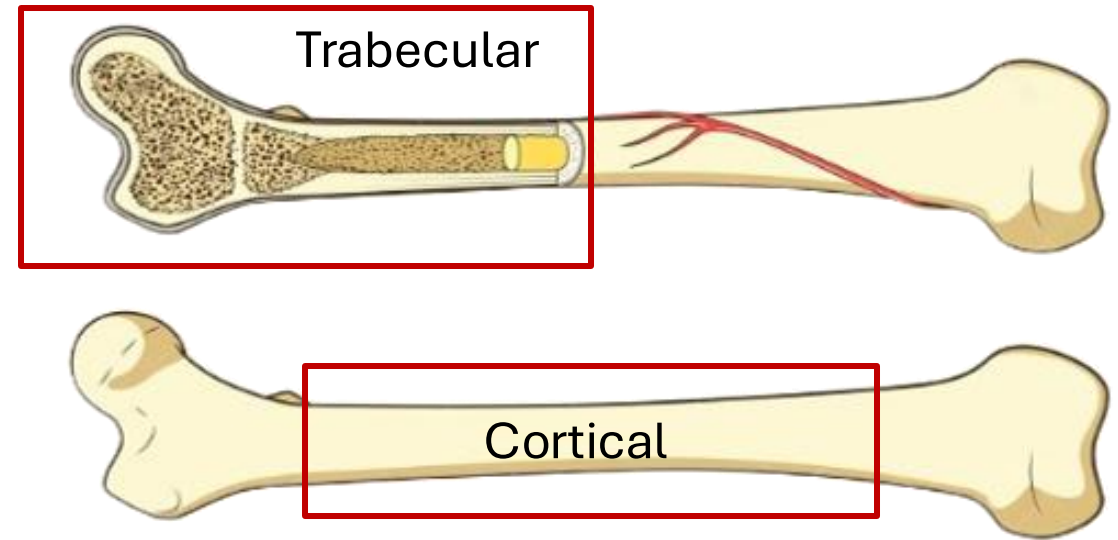


The Effect of Menopause on Osteoporosis and Bone Degeneration

Osteoporosis: a bone loss disease

Structural Impact

- Loss of bone density
 - Higher risk of serious fractures

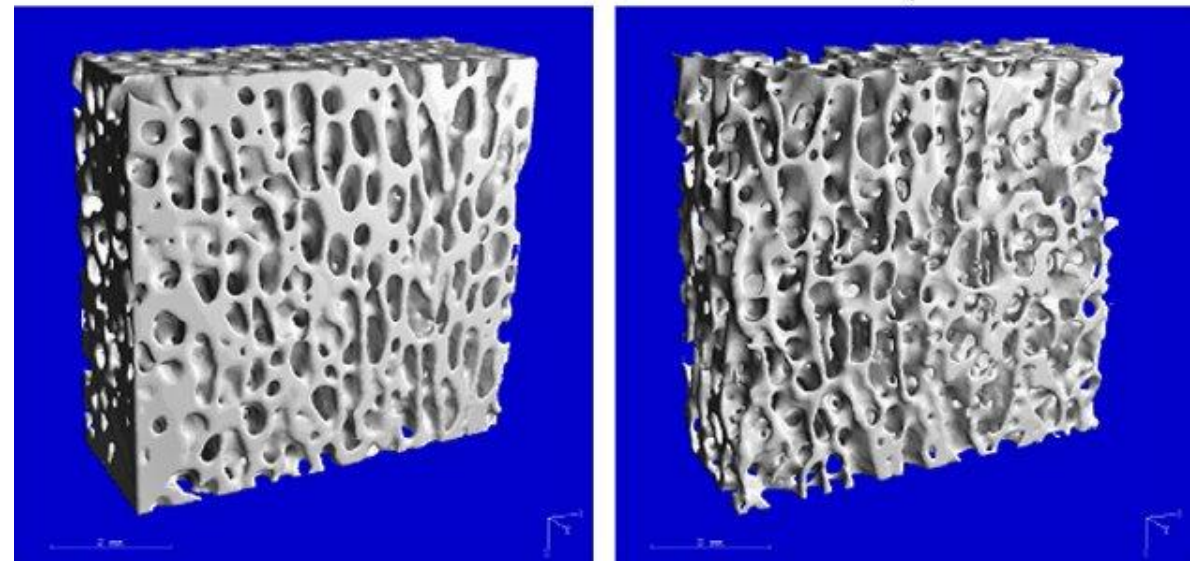
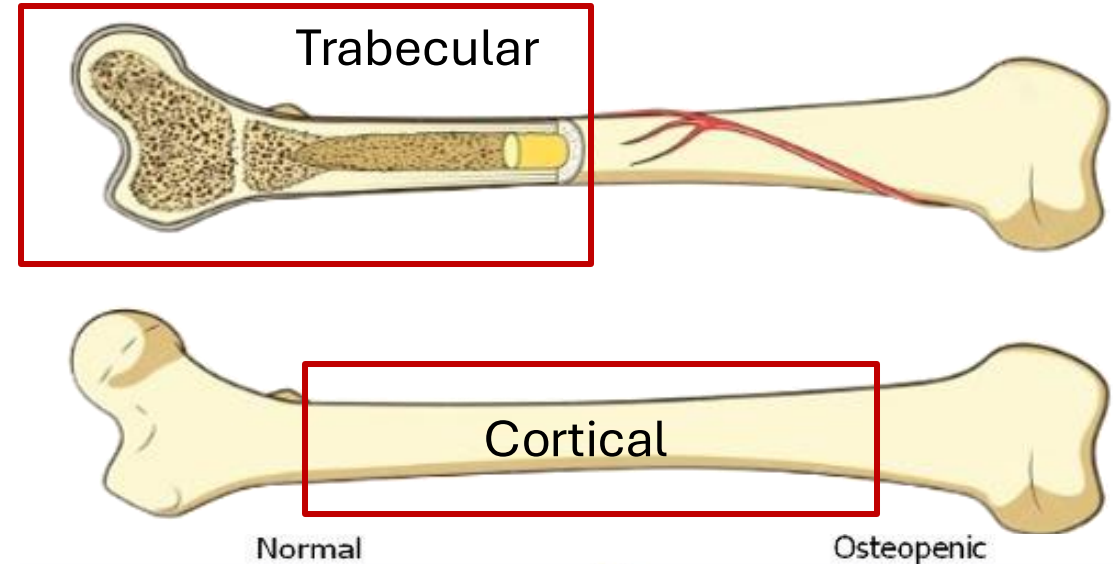


The Effect of Menopause on Osteoporosis and Bone Degeneration

Osteoporosis: a bone loss disease

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 - Trabecular bone becomes thin and porous



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Mechanical Impact

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 - Reduction in the bone's ability to bear weight and resist stress

The Effect of Menopause on Osteoporosis and Bone Degeneration

Osteoporosis: a bone loss disease

Structural Impact

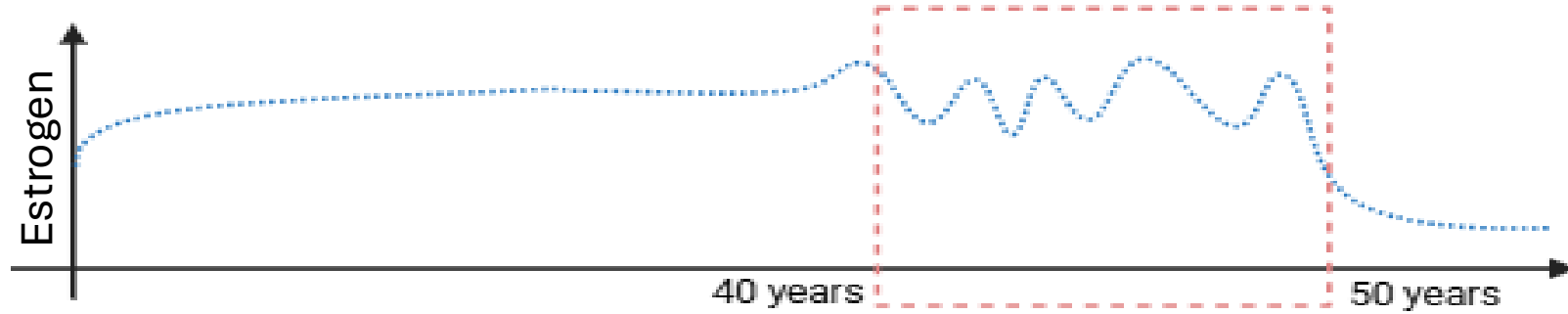
- Loss of bone density
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Mechanical Impact

- Loss of stiffness and strength
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Bone Reabsorption > Bone Formation

Estrogen Throughout Human life



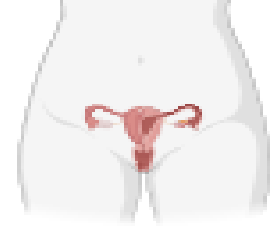
40 years

50 years

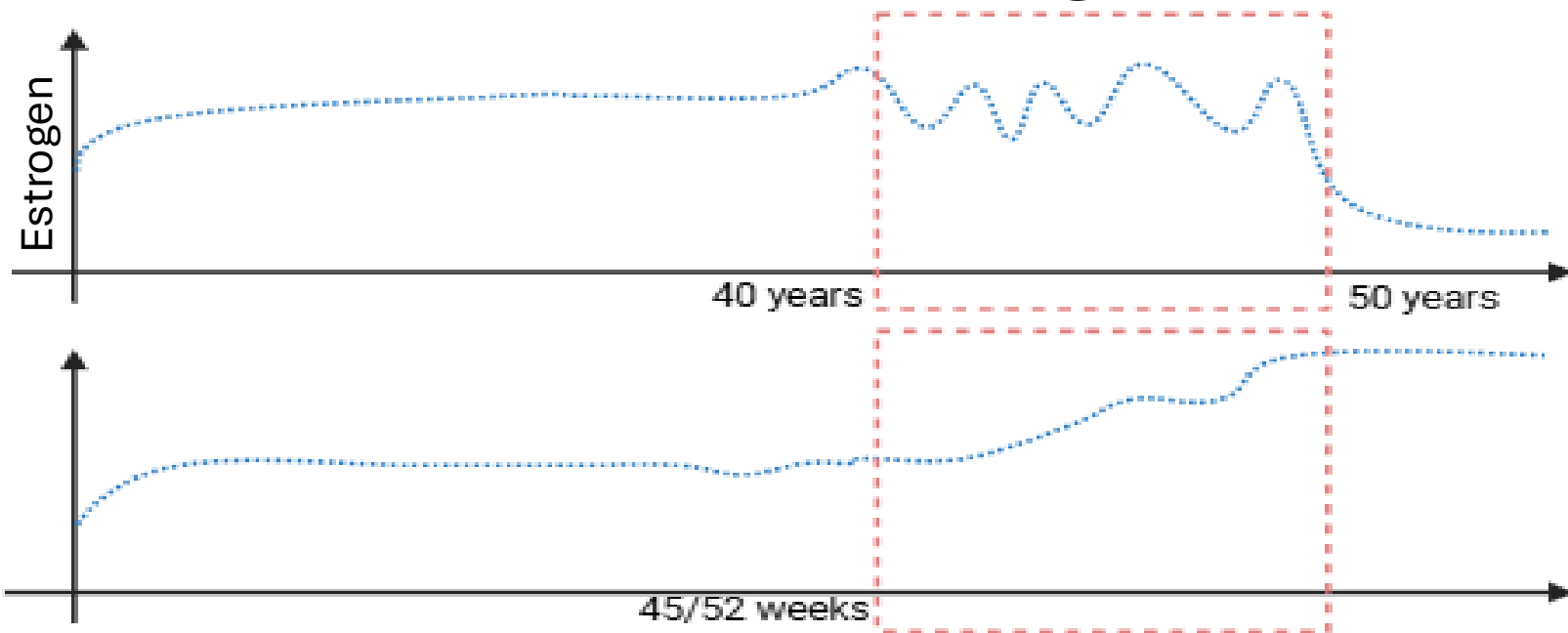
Perimenopause

Menopause

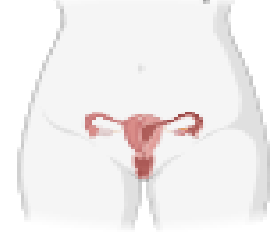
Human Menopause



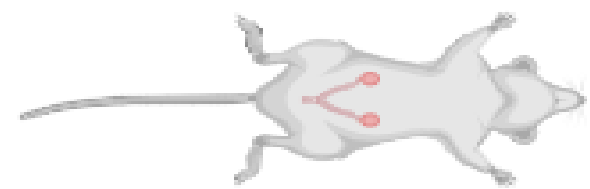
Estrogen in Mice



Human Menopause

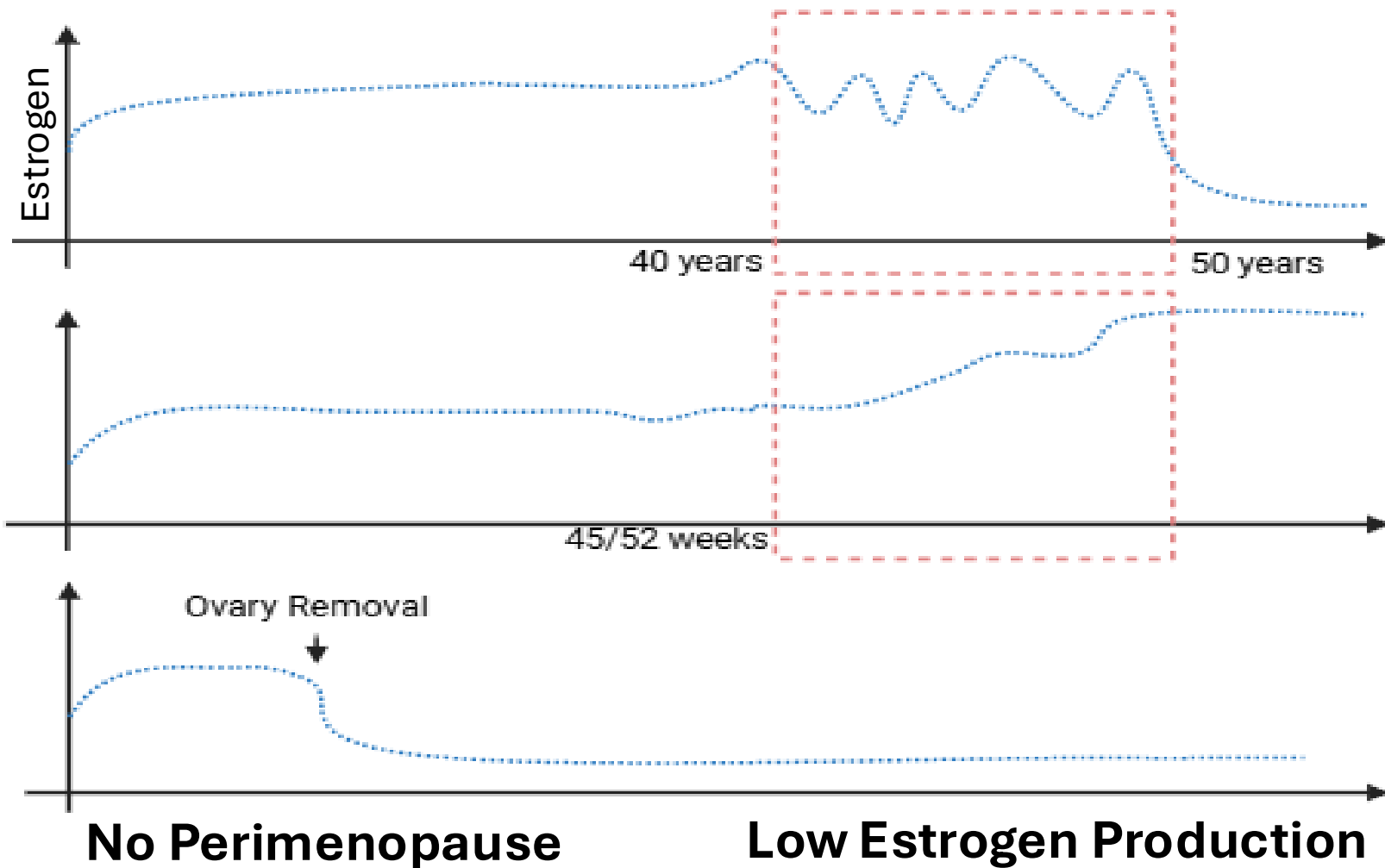


Mouse Reproductive Senescence

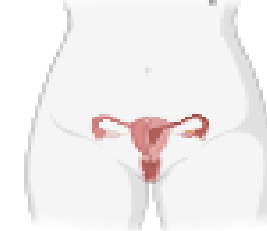


No Perimenopause or Menopause

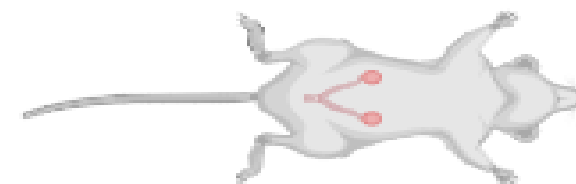
Removal of Ovaries



Human Menopause



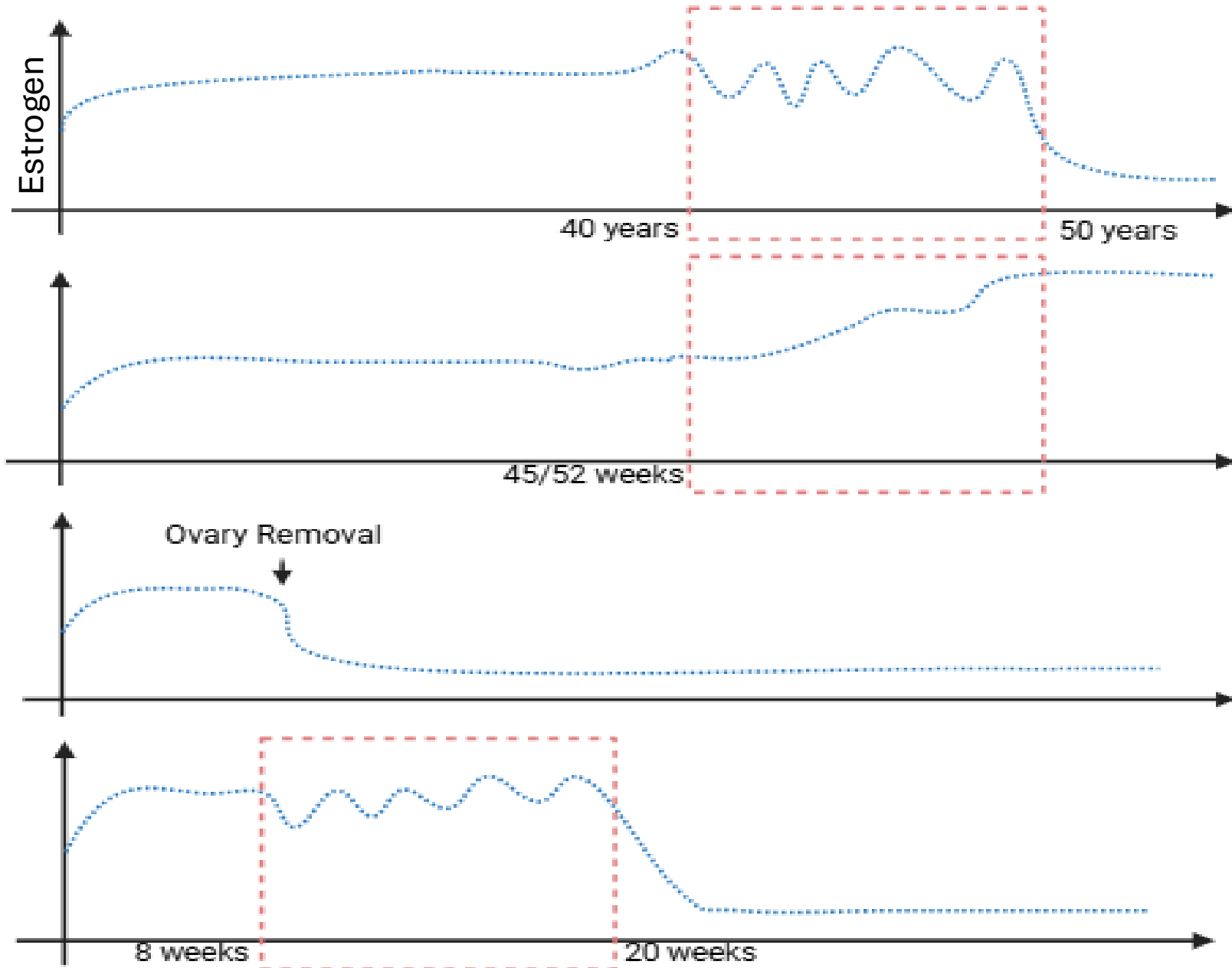
Mouse Reproductive Senescence



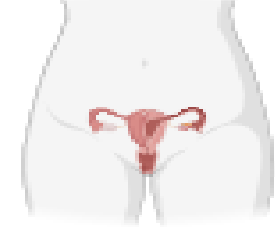
Mouse Ovariectomy



Chemically Induced Menopause with 4-vinylcyclohexane (VCD)



Human Menopause



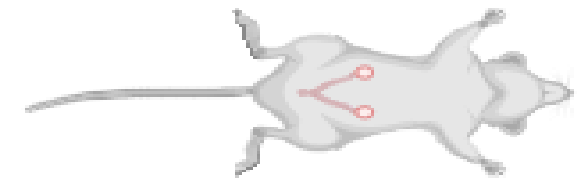
Mouse Reproductive Senescence



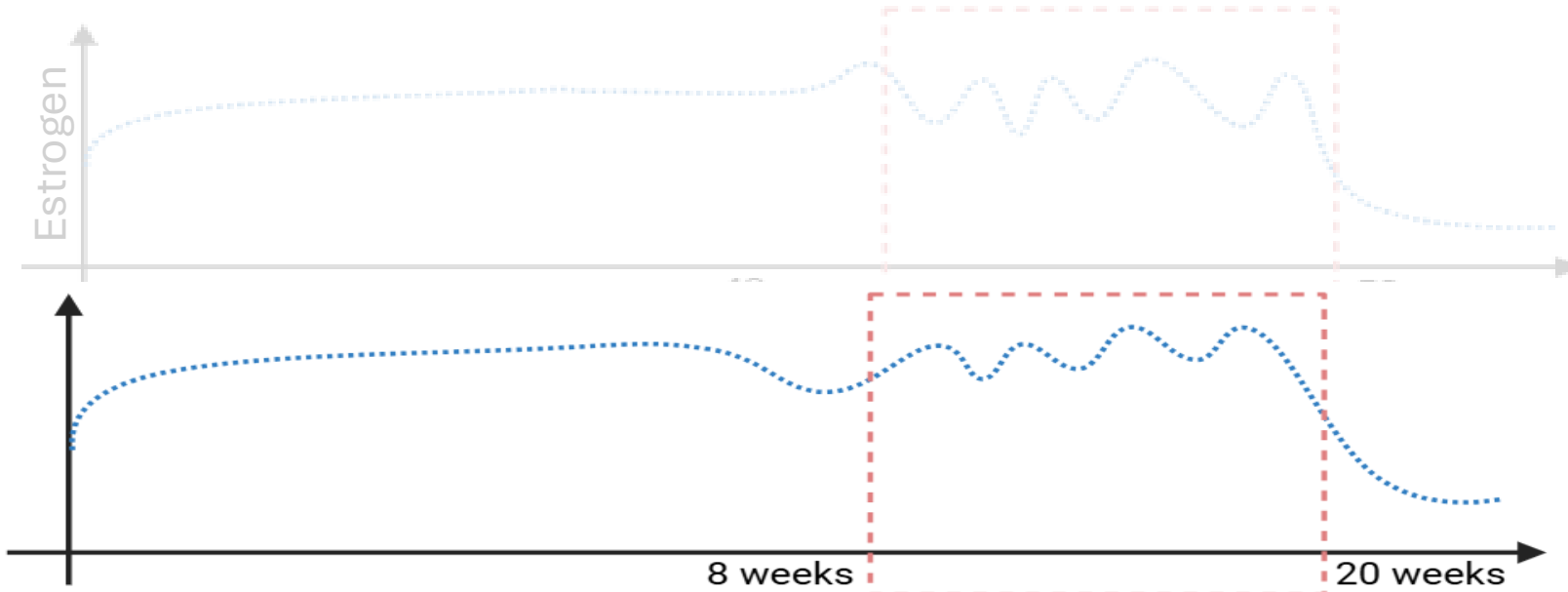
Mouse Ovariectomy



Acute Ovarian Failure (VCD)



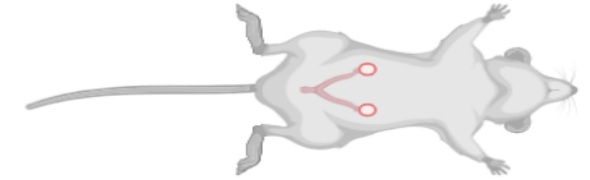
Modeling Menopause and Osteoporosis in Mice



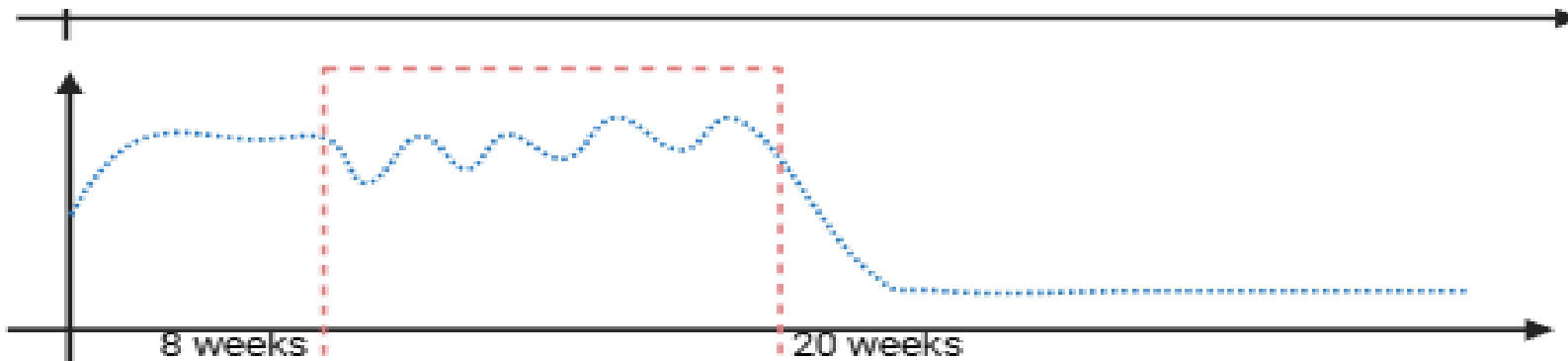
Human Menopause



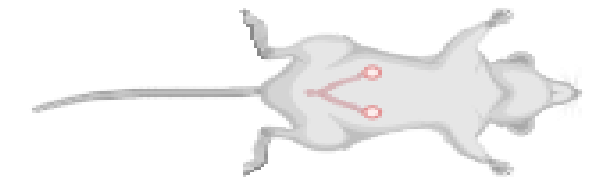
Acute Ovarian Failure (VCD)



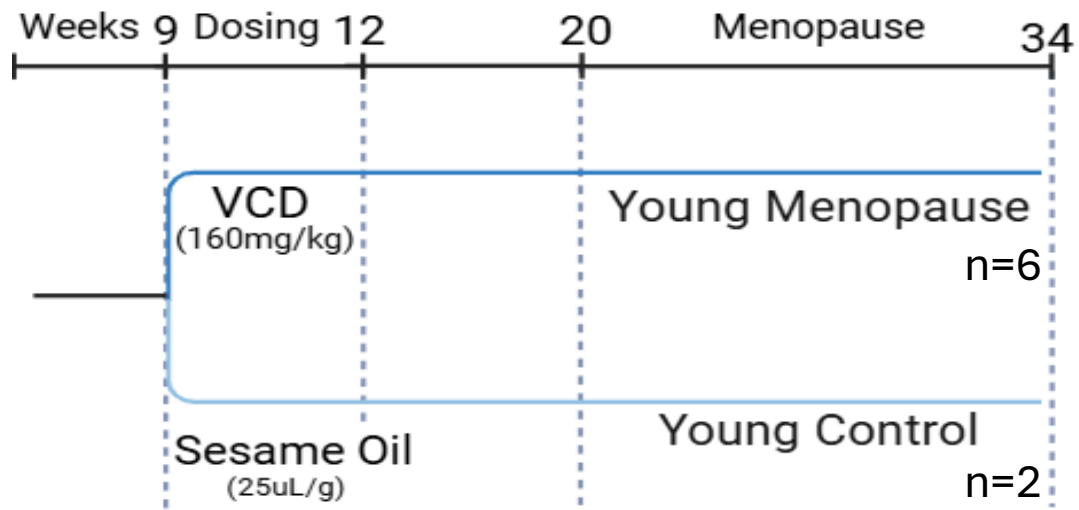
Hypothesis: Osteoporosis presents differently depending on the age at which menopause is induced, leading to distinct structural and mechanical changes in bone.



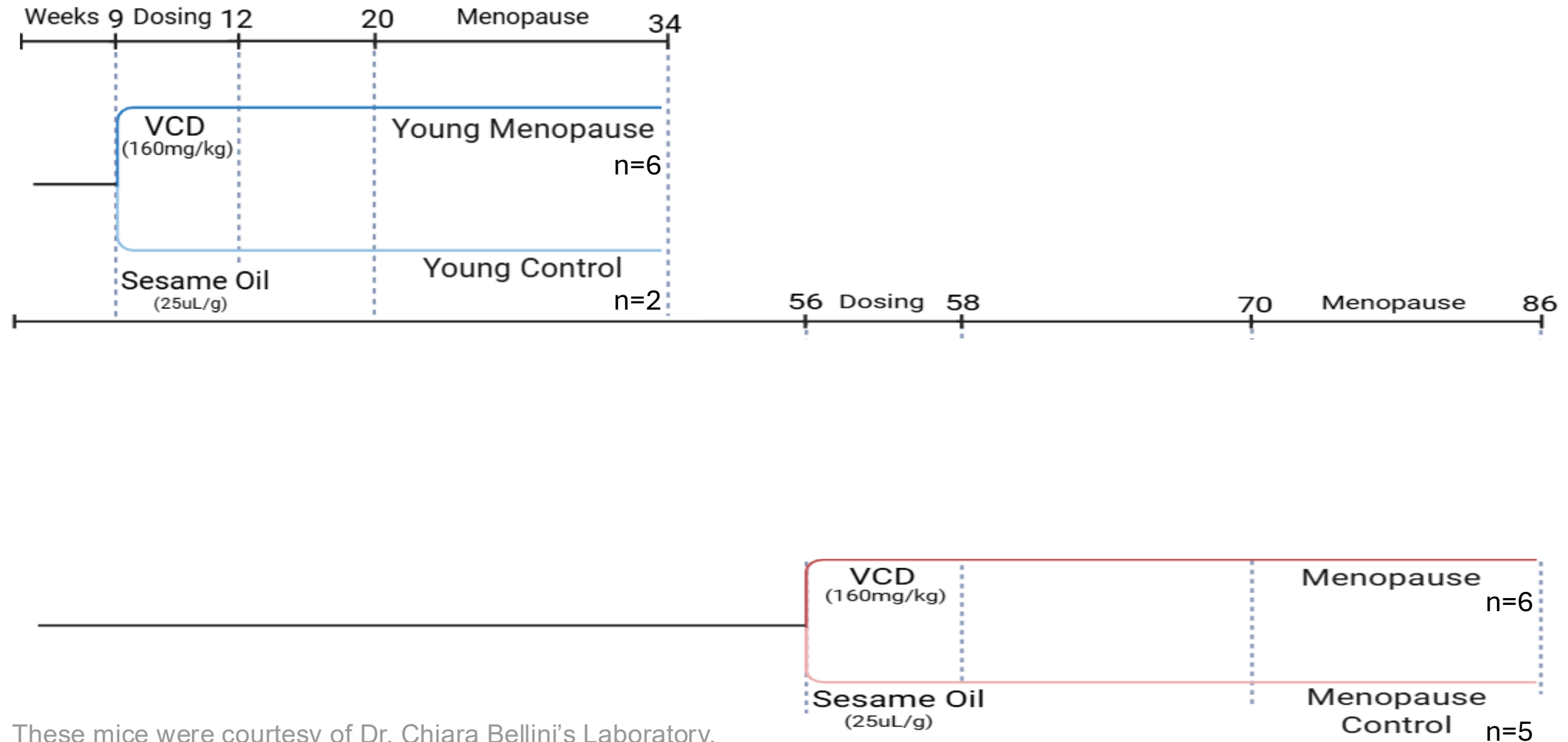
Acute Ovarian Failure (VCD)



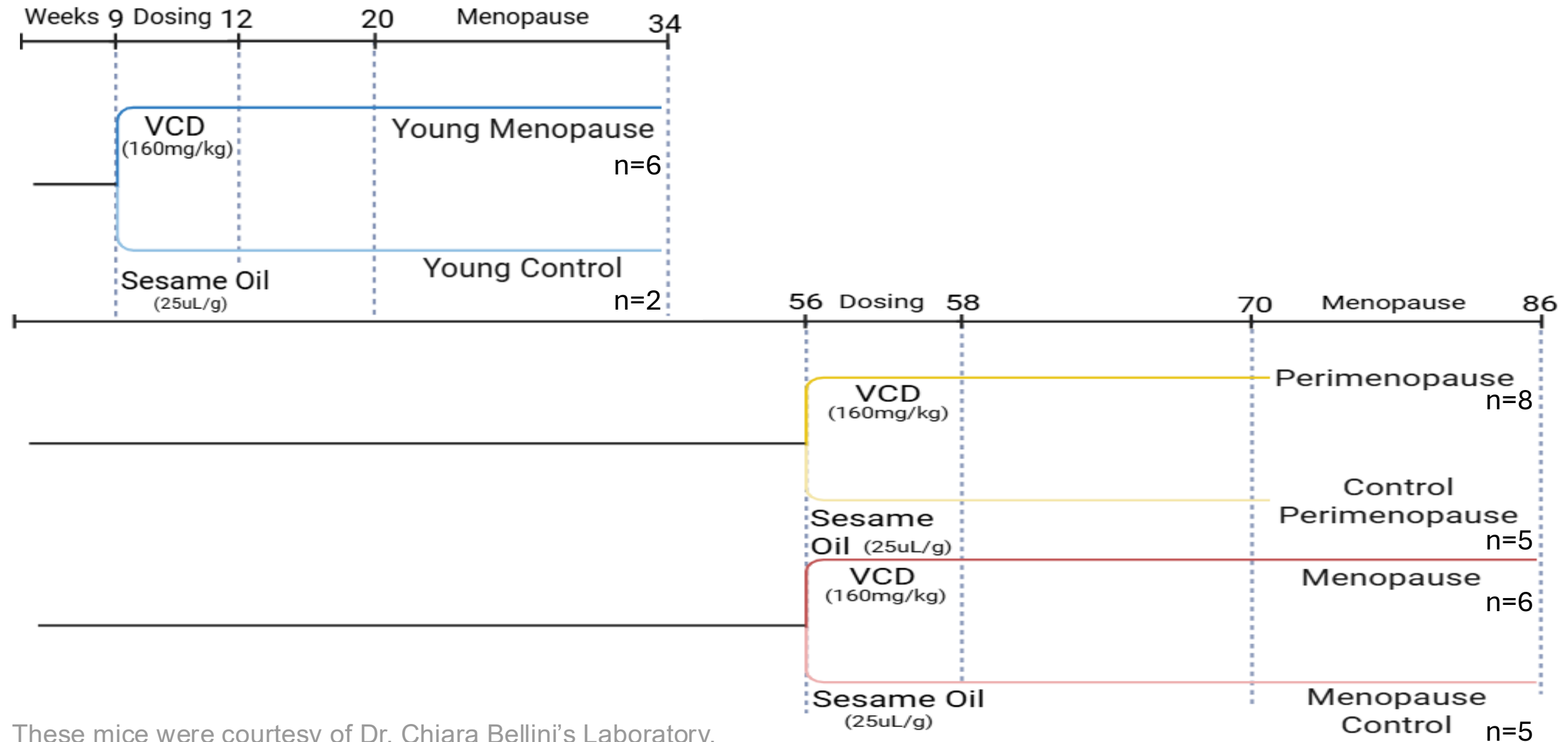
Isolating the Effects of Menopause with Aging



Isolating the Effects of Menopause with Aging



Isolating the Effects of Menopause with Aging



These mice were courtesy of Dr. Chiara Bellini's Laboratory.

Study of Skeletal Structure

Structural Study

Mechanical Study

Methods

Study of Skeletal Structure

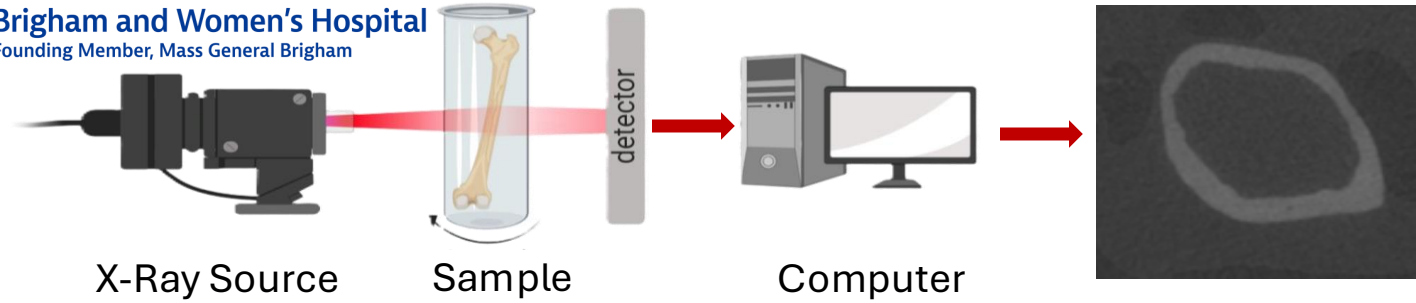
MicroCT
Structural Study

Mechanical Study

Methods

Study of Skeletal Structure

 Brigham and Women's Hospital
Founding Member, Mass General Brigham



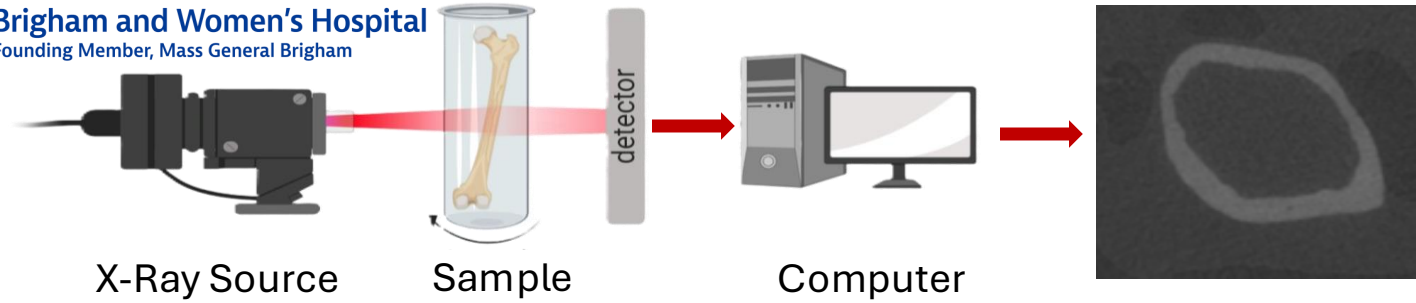
MicroCT
Structural Study

- 3D image of bone is captured

Methods

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MicroCT Structural Study

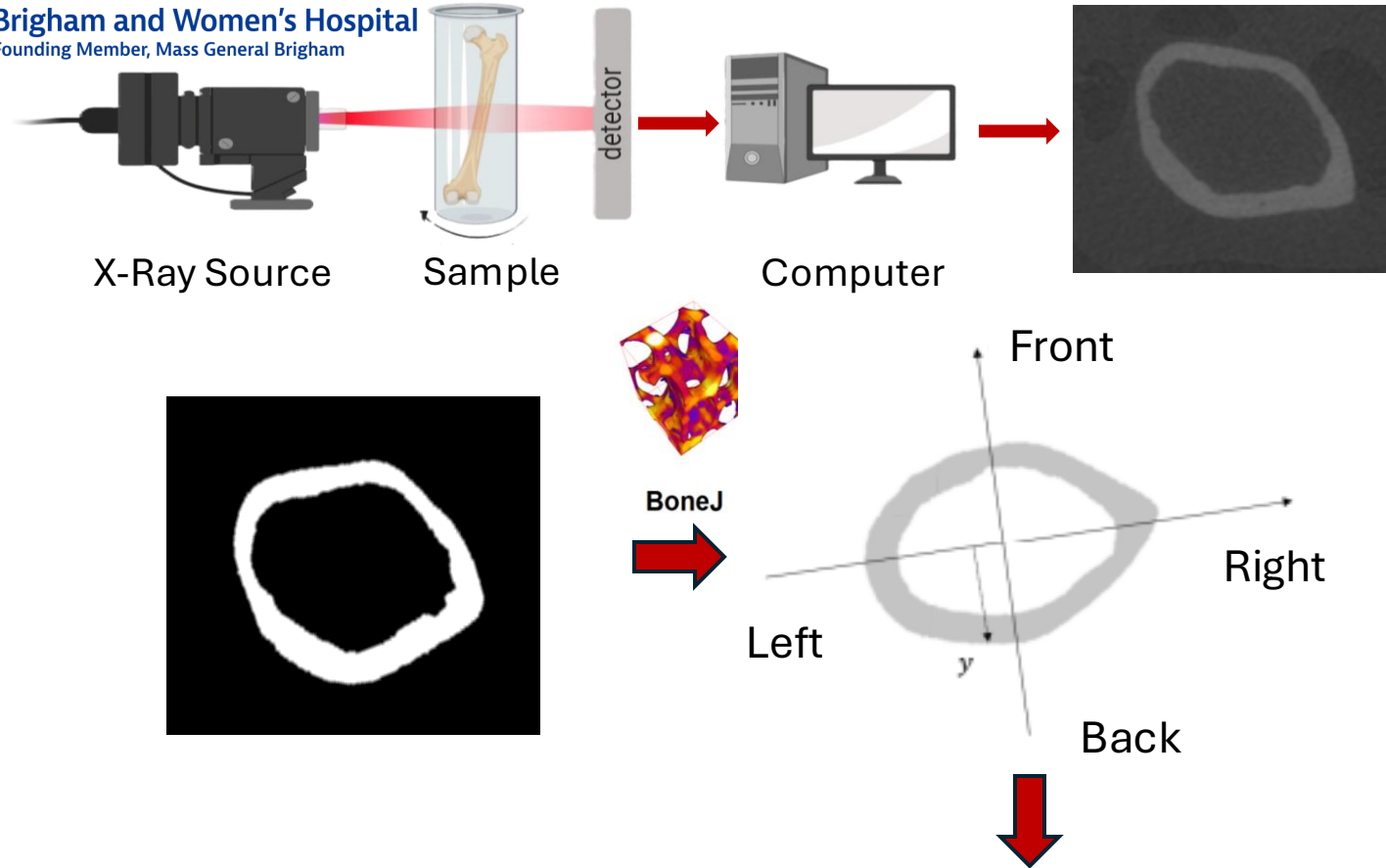
- 3D image of bone is captured
- Images are processed for contrast and clarity



Methods

Study of Skeletal Structure

Brigham and Women's Hospital
Founding Member, Mass General Brigham



MicroCT Structural Study

- 3D image of bone is captured
- Images are processed for contrast and clarity
- Geometrical properties of each slice are calculated with BoneJ

	Label	Bone Code	Slice	CSA (mm ²)	X cent. (mm)	Y cent. (mm)	Density	wX cent. (mm)	wY cent. (mm)	Theta (rad)	R1 (mm)	R2 (mm)	Imin (mm ⁴)	Imax (mm ⁴)	Ip
4	V3YLFThre	0	4	0.018	3.079	2.265	1.8	3.079	2.265	-0.874	0.078	0.091	4.02E-05	1.71E-05	

Methods

Study of Material

MicroCT

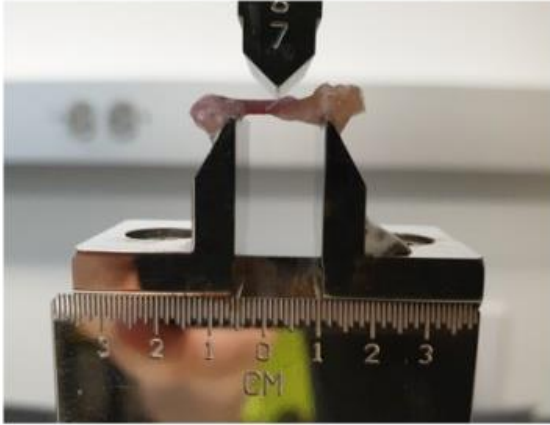
Structural Study

3 Point Bending

Mechanical Study

Methods

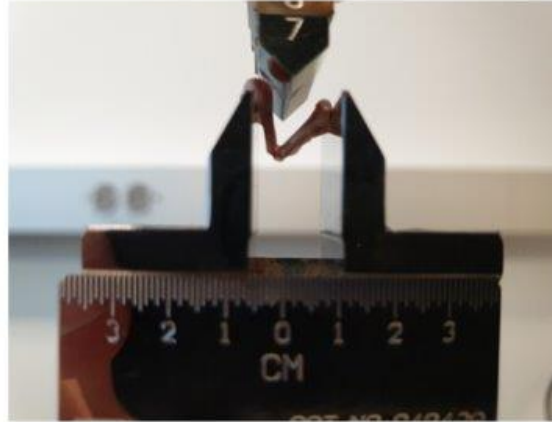
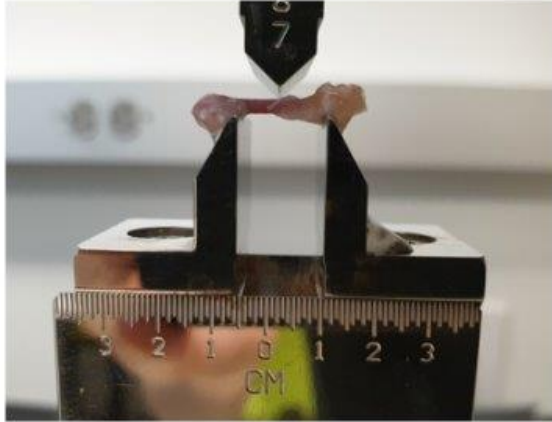
Study of Material



3 Point Bending
Mechanical Study

Methods

Study of Material

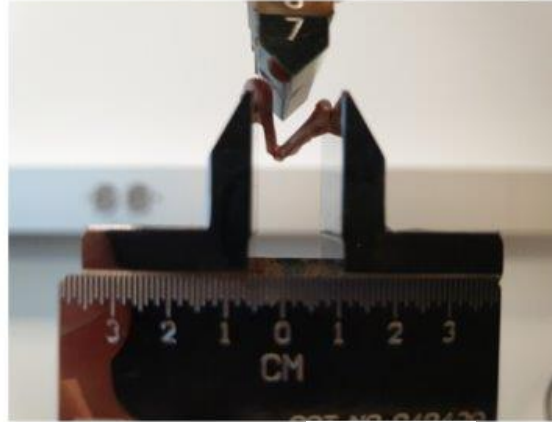
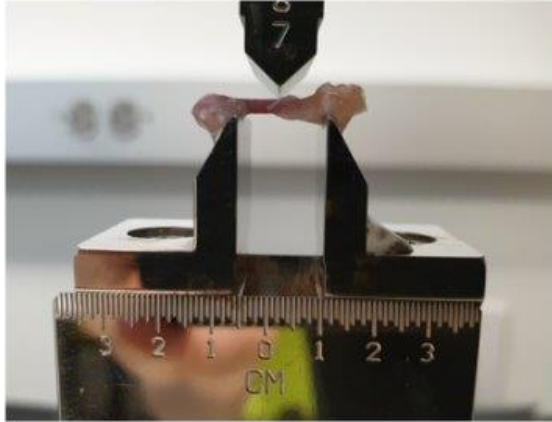


3 Point Bending Mechanical Study

- Record force (N) being experienced by the bone at a set rate of displacement (mm/sec)

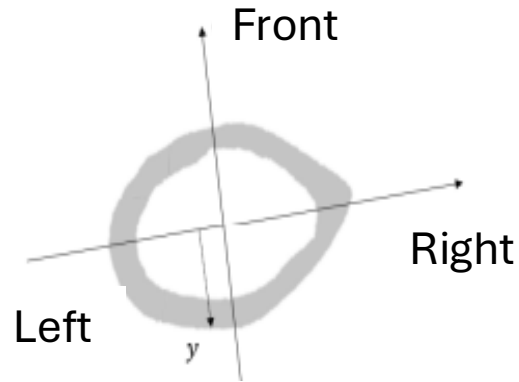
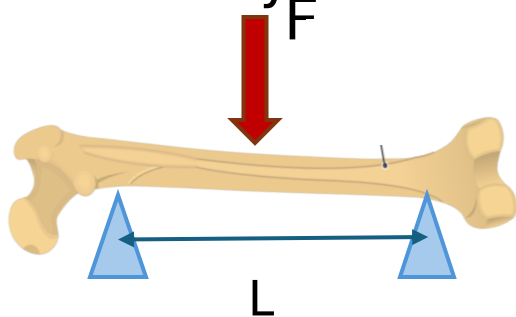
Methods

Study of Material



3 Point Bending Mechanical Study

Beam Theory



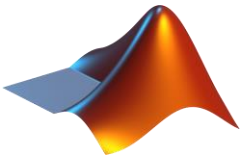
Stress

$$\sigma_{\max} = \frac{-yFL}{4I_y}$$

Strain

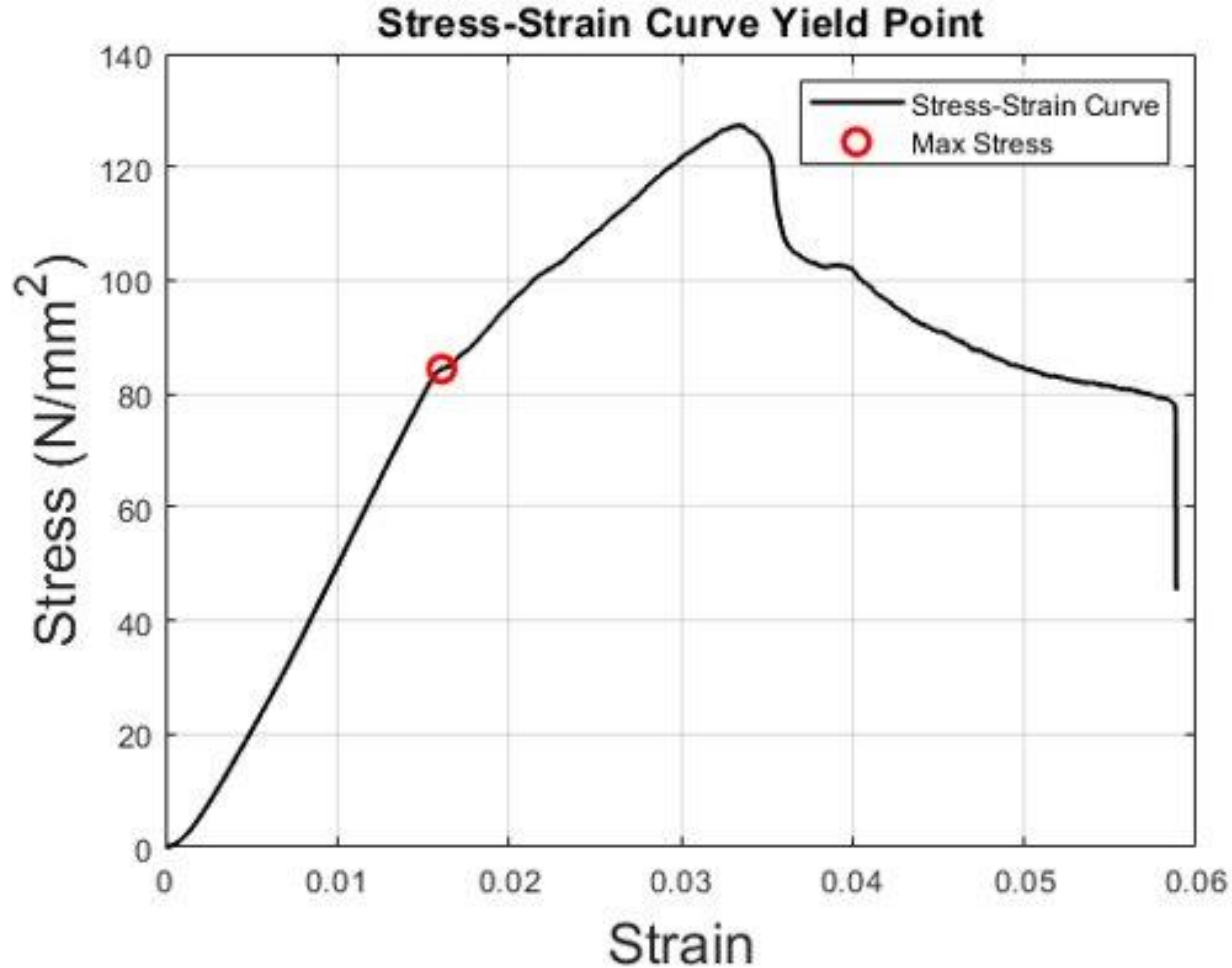
$$\epsilon_{\max} = \frac{12v_{\max}y}{L^2}$$

- Record force (N) being experienced by the bone at a set rate of displacement (mm/sec)
- Beam bending equations combined with MicroCT in MATLAB



Methods

Study of Material

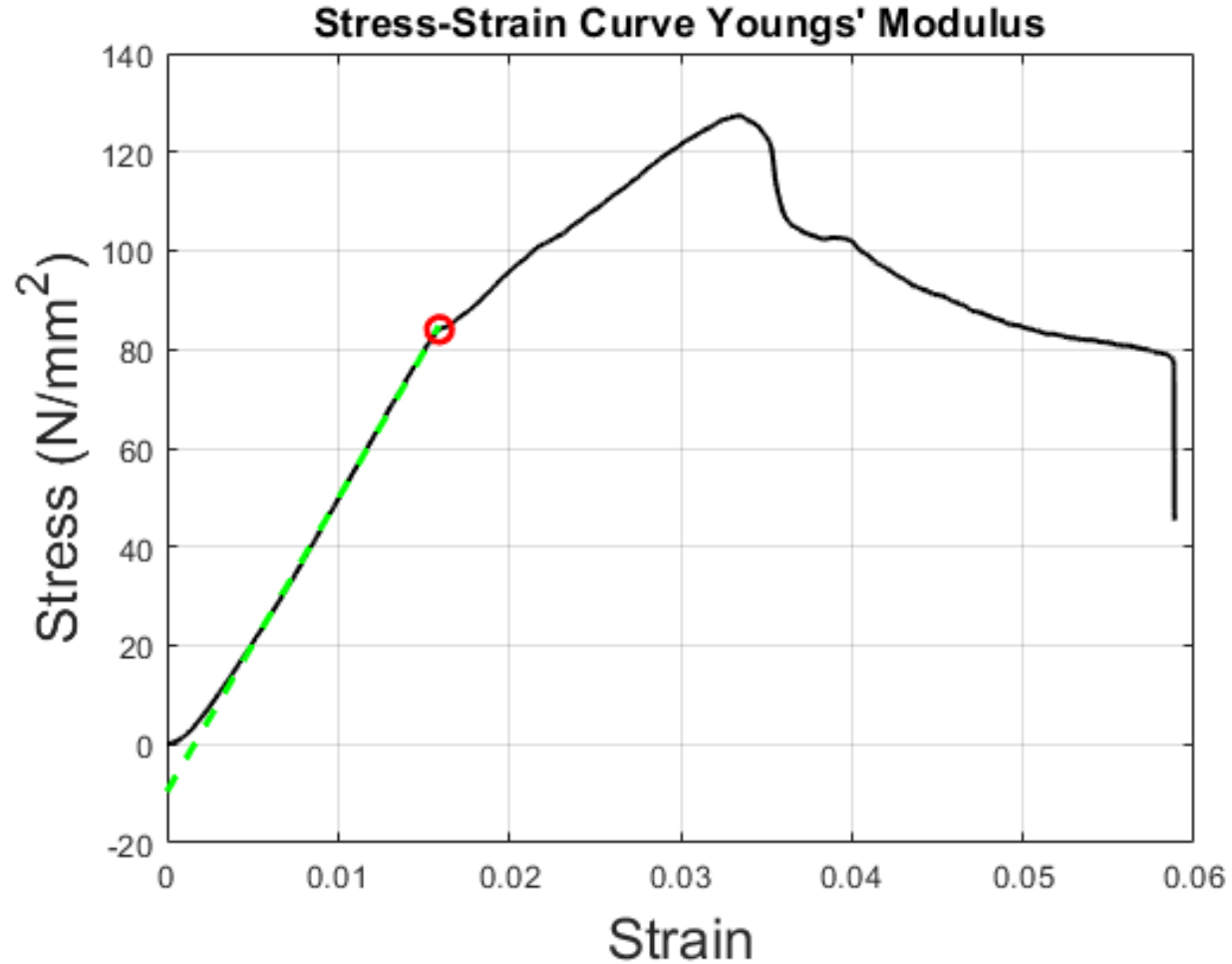


3 Point Bending Mechanical Study

- Stress-Strain Curve Plotted with MATLAB
- **Yield Point (σ_y)**- Moment where damage starts to occur

Methods

Study of Material

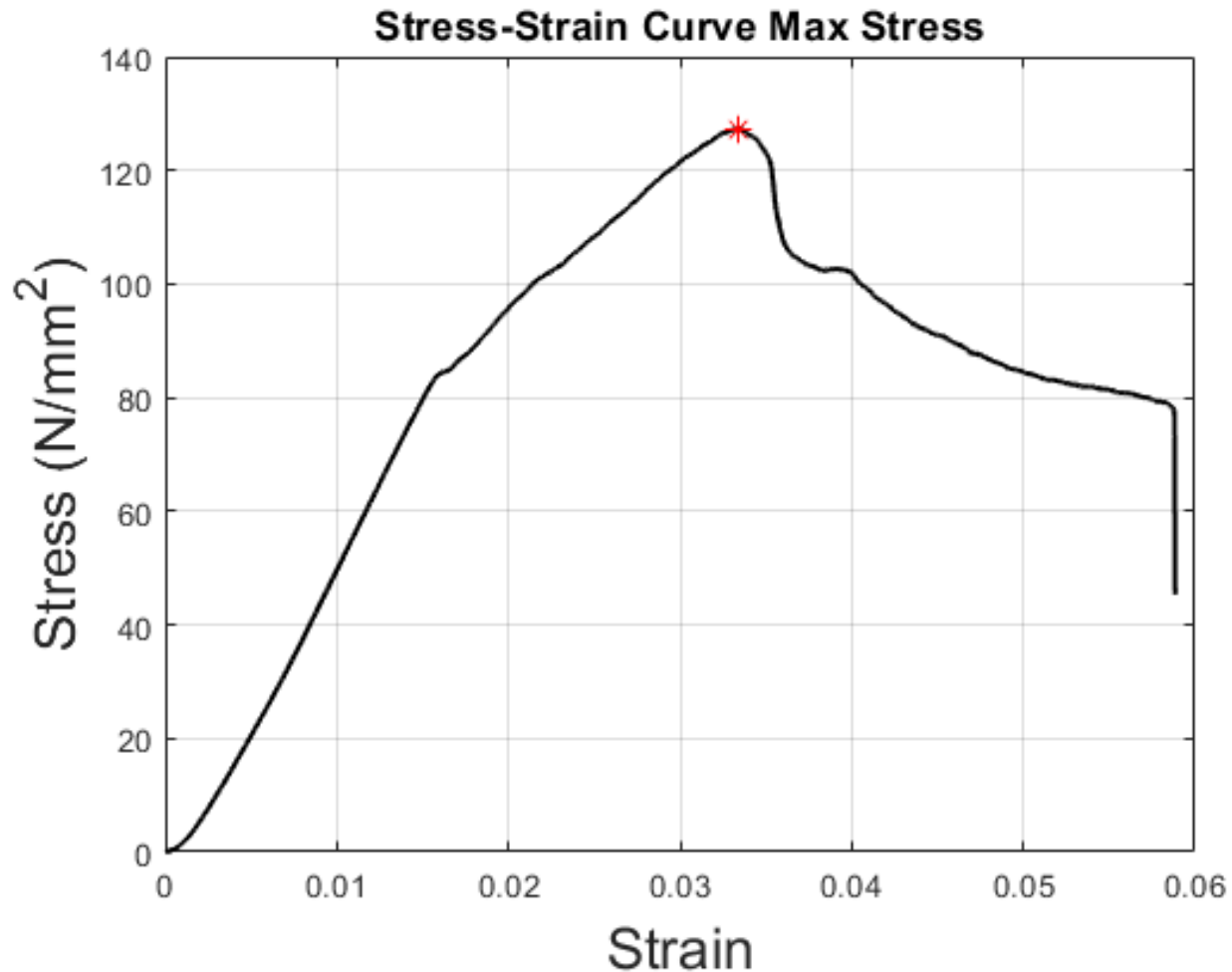


3 Point Bending Mechanical Study

- Stress-Strain Curve Plotted with MATLAB
- **Yield Point (σ_y)**- Moment where damage starts to occur
- **Young's Modulus (E)**- Slope of linear region

Methods

Study of Material

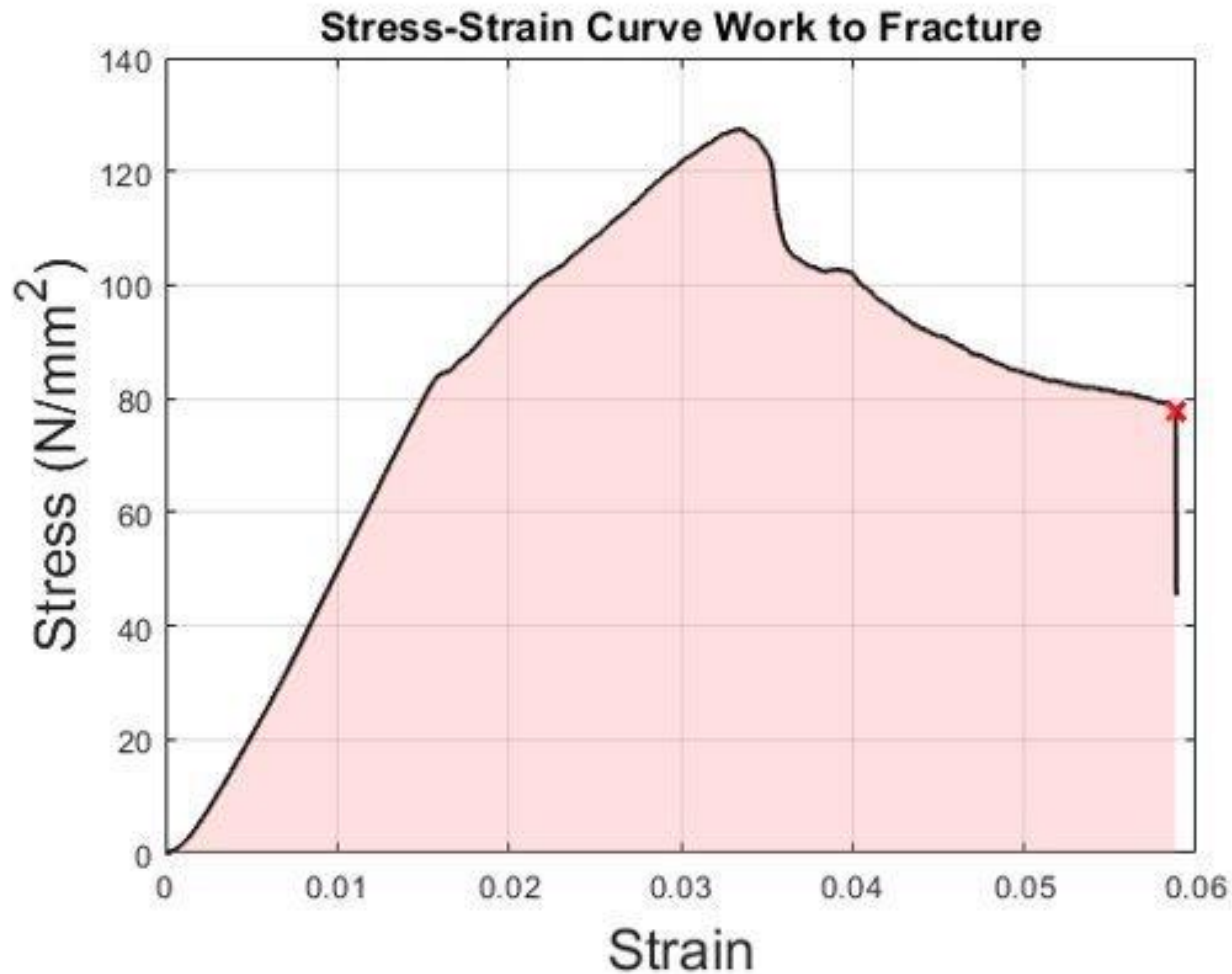


3 Point Bending Mechanical Study

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- **Yield Point (σ_y)**- Moment where damage starts to occur
- **Young's Modulus (E)**- Slope of linear region
- **Ultimate Stress (σ_{max})**- Maximum stress

Methods

Study of Material

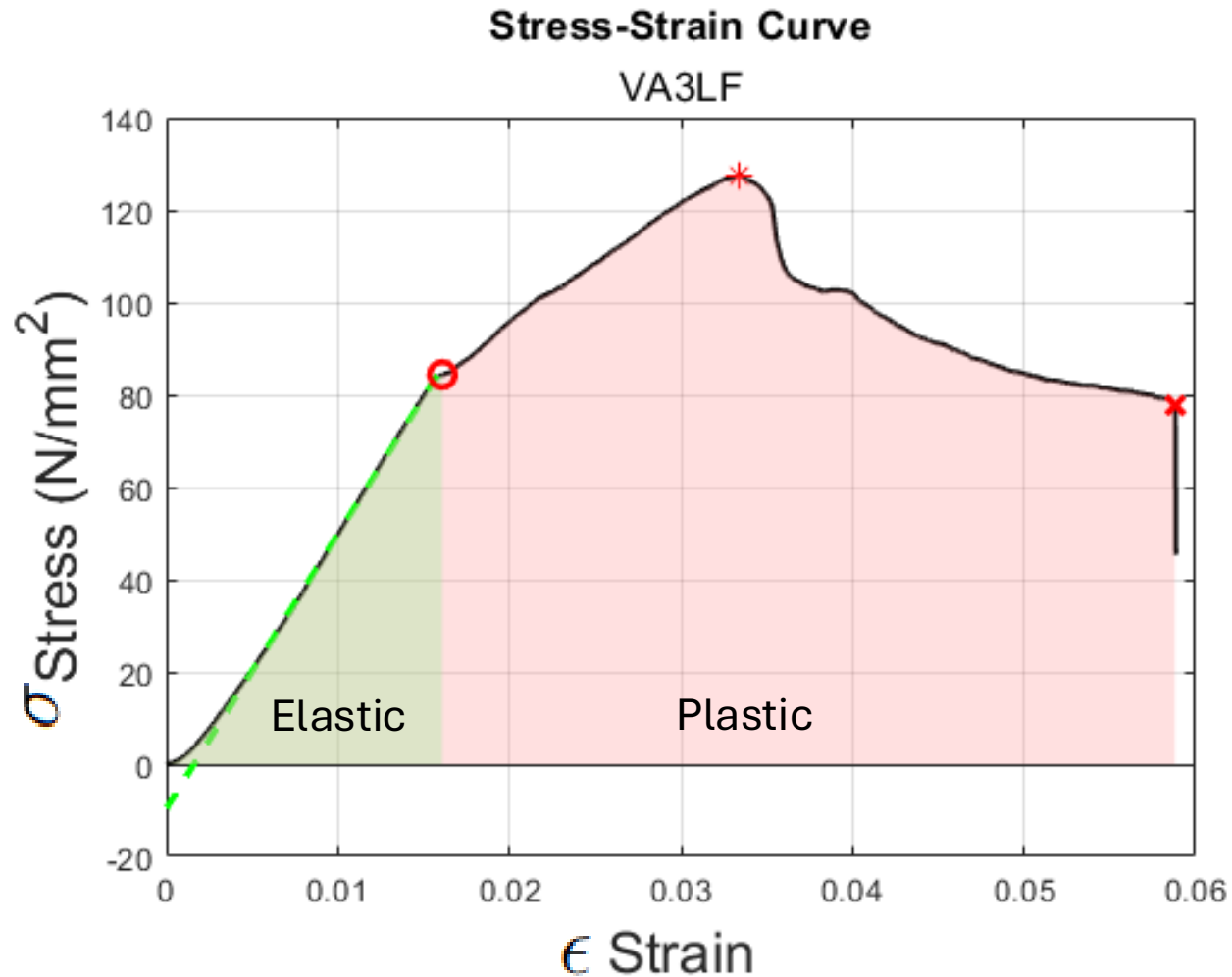


3 Point Bending Mechanical Study

- Stress-Strain Curve Plotted with MATLAB
- **Young's Modulus (E)**- Slope of linear region
- **Yield Point (σ_y)**- Moment where damage starts to occur
- **Ultimate Stress (σ_{\max})**- Maximum stress
- **Work to Fracture (WF)**- Total area under the curve

Methods

Study of Material



3 Point Bending Mechanical Study

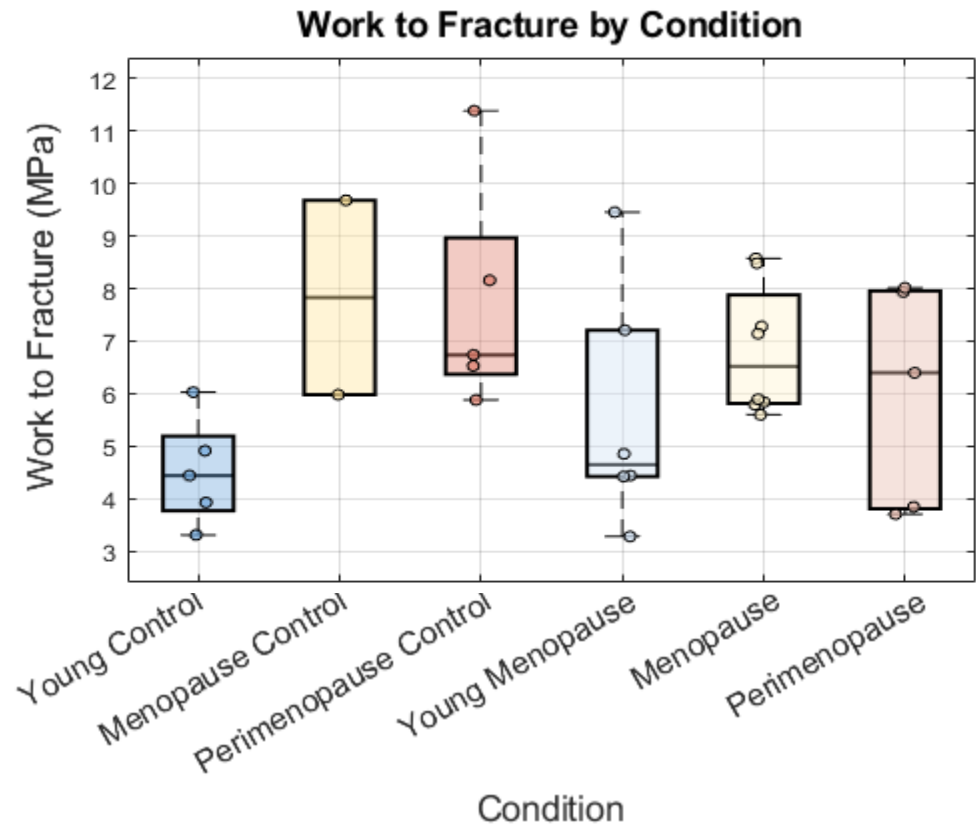
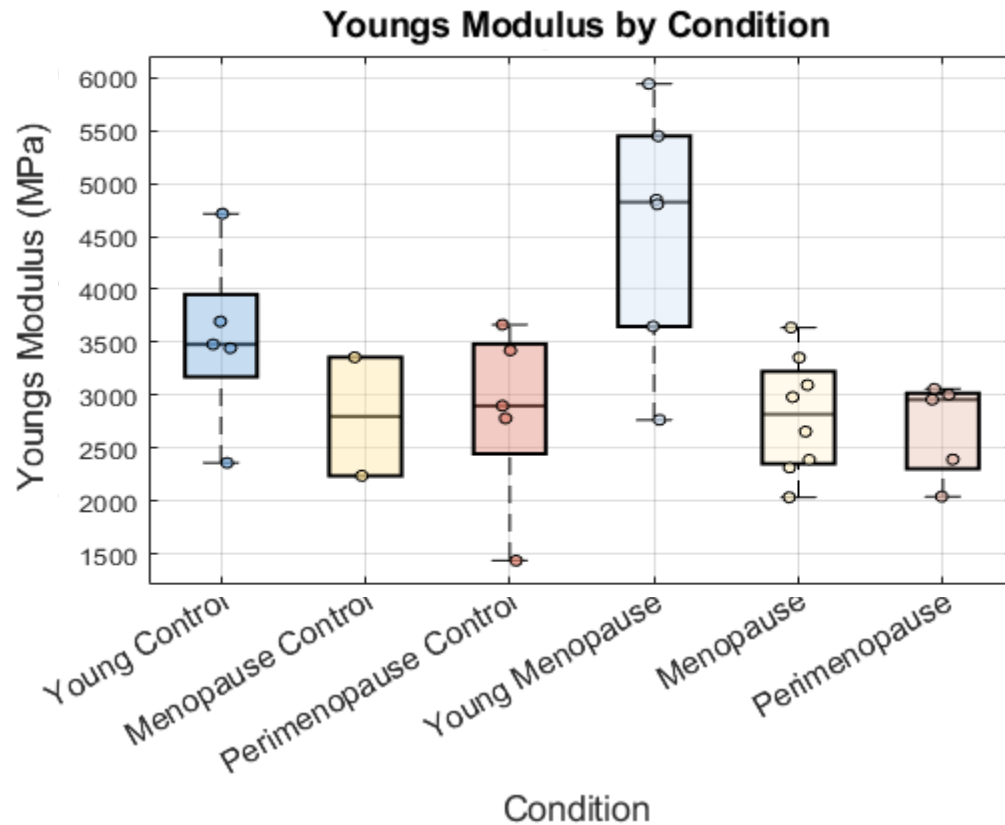
Stress-Strain Curve Plotted with MATLAB
Young's Modulus (E)- Slope of linear region

Yield Point (σ_y)- Moment where damage starts to occur

Ultimate Stress (σ_{\max})- Maximum stress

Work to Fracture (WF)- Total area under the curve

Results

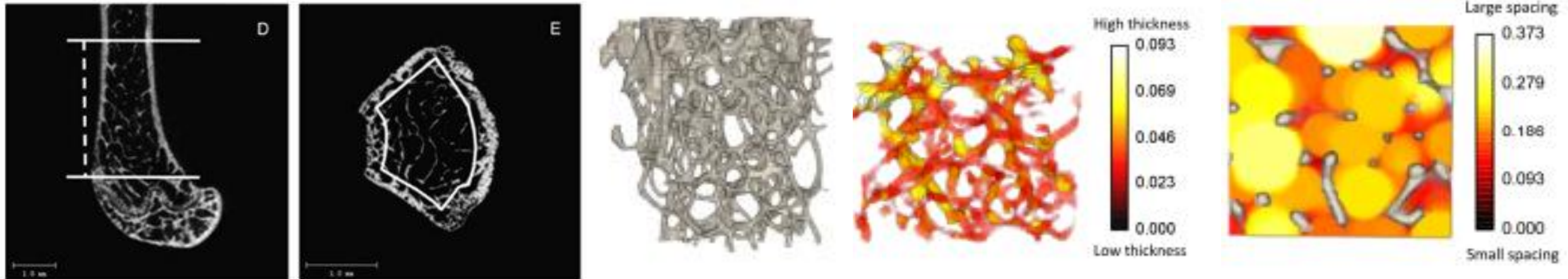


- Average Young's Modulus (E) was higher in the treated mice from young menopause (YM) and perimenopause (PM)
- There was a greater spread of data in YM compared to all other conditions.

- Young Control (YC) and YM has a lower Work to Fracture (WF) than other conditions
- PM and Menopause (M) shows similar mean WF values, which are both lower than controls and higher than YM

Future Work

Analysis can be done on trabecular region with boneJ to identify changes in thickness and density of inner bone



More members each condition will be analyzed with the same imaging and mechanical testing methods for statistical significance

Thank you



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In collaboration with

The mice used in this study were contributed by the
Dr. Chiara Bellini Bioengineering Lab

MicroCT imaging done in

Dr. Julia Charles Lab



Hannah Wilker
Masters Student



Amanda Dias
PhD Student

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Founding Member, Mass General Brigham