Skeletal Organoid Bioreactor

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Background (Motivation)

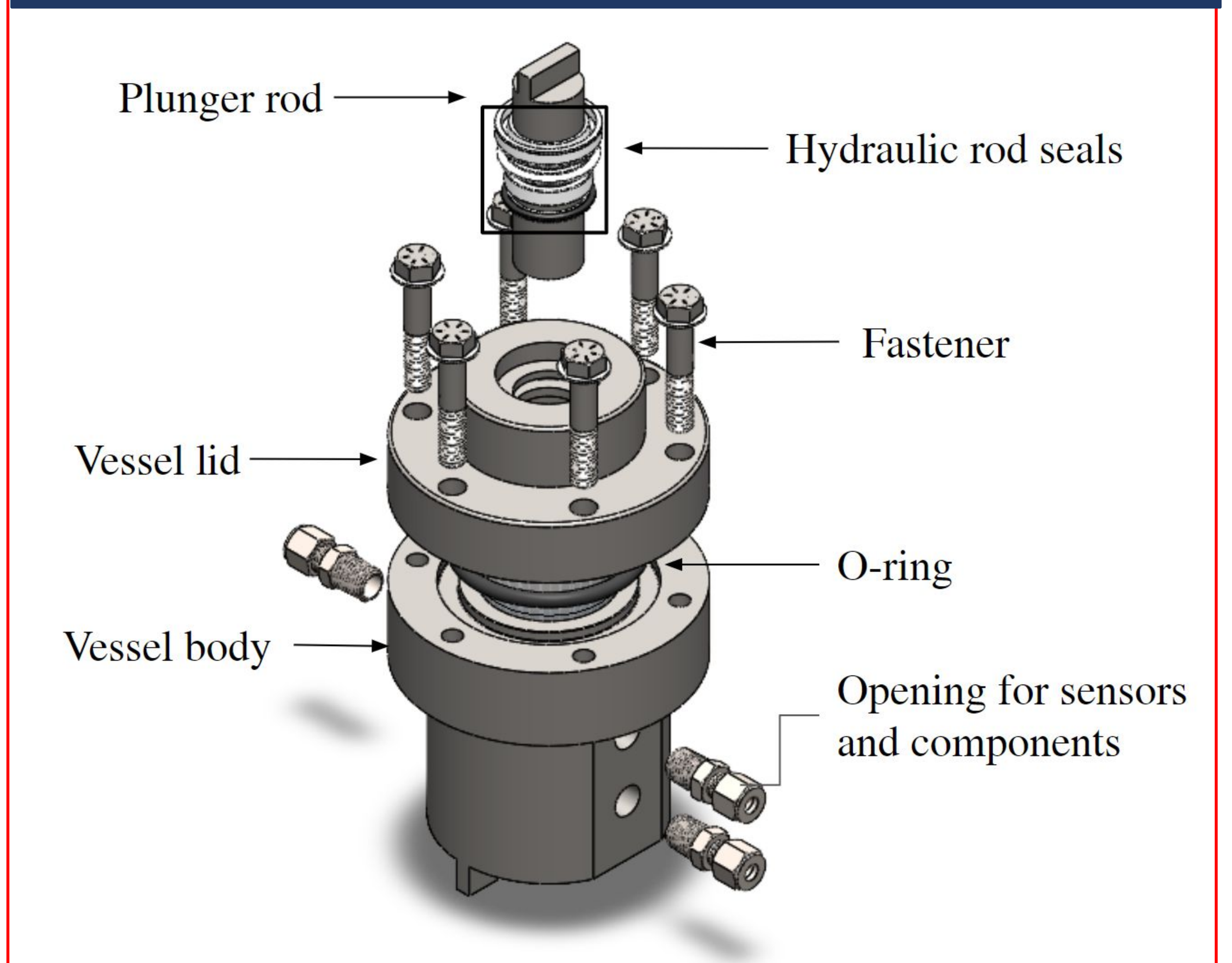
Motivation: To support research in developing cartilage with better mechanical properties to devise better treatments for cartilage degradation.

Approach: Current methods grow cartilage organoids in a stress-free environment. This project seeks to create a bioreactor that uses a hydraulic force machine to apply cyclic hydrostatic pressure to the cells during growth.

Problem Statement

To design a bioreactor capable of holding a bag of cells in water at 37°C with cyclic hydrostatic pressure up to 1500 psi at 1 Hz

Design Overview / Challenges



Bioreactor Components

Primary challenge: Withstanding high pressure (1500 psi)
Secondary challenge: Maintaining temperature (36-37°C)
Design features:

- No welded components to avoid specialized welding requirements and costs for high pressure systems
- Utilizes hydraulic cylinder seals rated for high pressures (< 2300 psi) to satisfy loading requirements
- High lid and wall thickness for factor of safety greater than 1.7
- Fasteners and seals selected to prevent failure at vessel lid and body interface
- Sweater crocheted for thermal insulation

Background Analysis

Force and Displacement

Spec. Vol. at 37°C and 1 atm: $0.0010066\frac{m^3}{kg}$

Spec. Vol. at 37°C and 10MPa: $0.001003\frac{m^3}{kg}$

Volume differential: $\frac{1006.6-1003}{1006.6} = 0.3576\%$

ΔVolume: $0.3576\% \times 240mL = 0.863mL$

Displacement: $\frac{0.863}{\pi r^2} = \frac{0.863}{\pi(1.27cm)^2} = 1.7mm$

Max Force: $PA = 1000\frac{N}{cm^2} \times 5.07cm^2 = 5,067N$

Force exerted on lid by pressure

Lid Force: $PA = 1000\frac{N}{cm^2} \times 15.2cm^2 = 15,201N$

Bolt Force: $15,201/6 = 2,533N$

Structure Analysis

Shell Thickness Calculations

Circumferential and Longitudinal Stress

$$t_{long} = \frac{PR_i}{S(E-0.6)P} = 0.11"$$

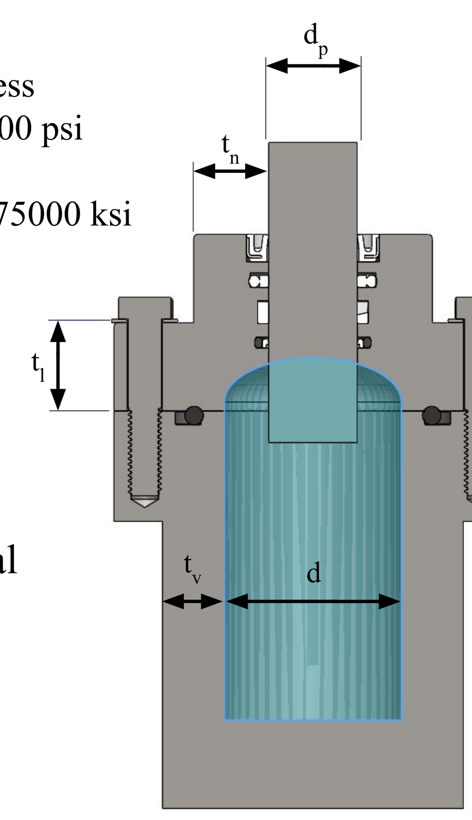
$$t_{circ} = \frac{PR_i}{2S(E+0.4)P} = 0.051"$$

$$K_c t_{long} = 0.396 \qquad n = \frac{t_{actual}}{3t_{long}} = 1.70$$

- t_v: vessel thickness
- P: pressure = 1500 psi
- R_i = 1.45”
- S: max stress = 75000 ksi
- E = 29000 ksi
- t_{actual} = 0.56”
- Max K_c = 3

ASME Chapter VIII Pressure Vessel Code:
“The primary plus secondary stresses and localized discontinuities shall be limited to S_{PS}, where S_{PS}=3S, and S is the maximum allowable stress of the material at temperature [and B > S where $B = \frac{0.125E}{(2R_0/t)}$]”

- t = 0.56”
- Ro = 3.5 in
- B = 517000 ksi
- S_{PS} = 75000*3 = 225000 ksi
- B > 225000
- **Safety Factor = B/S_{PS} = 2.3**



Lid Thickness Calculations

ASME Chapter VIII Pressure Vessel Code Standards:

UG-34 - Lid thickness w/o stress concentration:

$$t = d\sqrt{\frac{CP}{SE} + \frac{1.9Wh_G}{SEd^3}}$$

- d: inner diameter = 2.9”
- C: joint factor = 0.3
- P: pressure = 1500 psi
- S: $stress_{max}$ = 75 ksi
- E: joint efficiency =1
- W: bolt load = 26573 lbf
- h_G: gasket line= 1.343”
- t_l = 0.531”

UG-39 Reinforcement of central holes in flat lids:

$$A = 0.5d_p t_v + t_v t_b(1 - f_{r1})$$

- d_p: piston diameter = 1”
- t_v: vessel thickness = .56”
- t_n: nozzle thickness = .86”
- f_{r1}: $\frac{UTS_{Nozzle}}{UTS_{Vessel}} = 1$
- A = 0.28 in^2
- $A_{applied}$: t_n * 2 * 1 = 1.72 in^2
- Safety factor: 6.124

Fastener Analysis

Bolt Stiffness

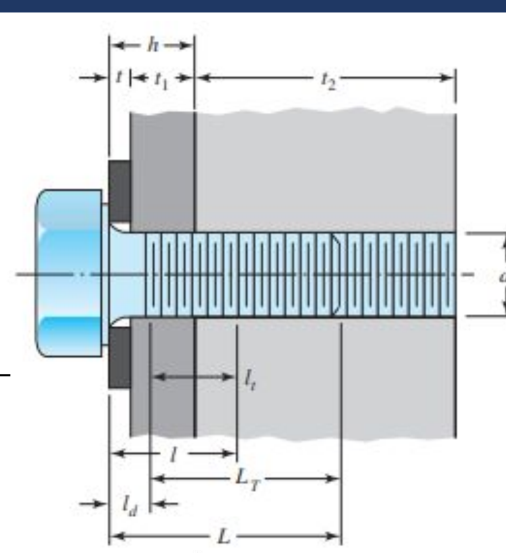
$$k_b = \frac{A_d A_t E}{A_d l_t + A_t l_d} = 2290\frac{kip}{in}$$

Material Stiffness

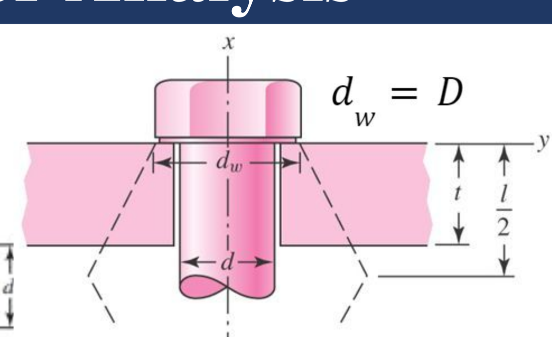
$$k_m = \frac{0.5774\pi Ed}{ln\frac{(1.155t+D-d)(D+d)}{(1.155T+D+d)(D-d)}} = 5177\frac{kip}{in}$$

Cyclic Loading Safety Factor

$$n_f = \frac{S_e(S_{UT}-\sigma_i)}{S_{UT}\sigma_a + S_e(\sigma_m - \sigma_i)} = 2.27$$



$$c = \frac{k_b}{k_b + k_m} = 0.31$$



$d_w = D$

Input Values	
S_e	$23.2ksi$ *
S_{UT}	$150ksi$
P_{max}	$1767.1lbf$
$F_i = 0.75F_p$	$6.975ksi$

*See Table 8-17

Pretension Coefficient

$$K = (\frac{d_m}{2})\frac{tan(\lambda)+f(sec(30))}{1-ftan(\lambda)sec(30)} + 0.625f_c = 0.2 \ *$$

*Corroborated with Table 8-15, K = 0.2

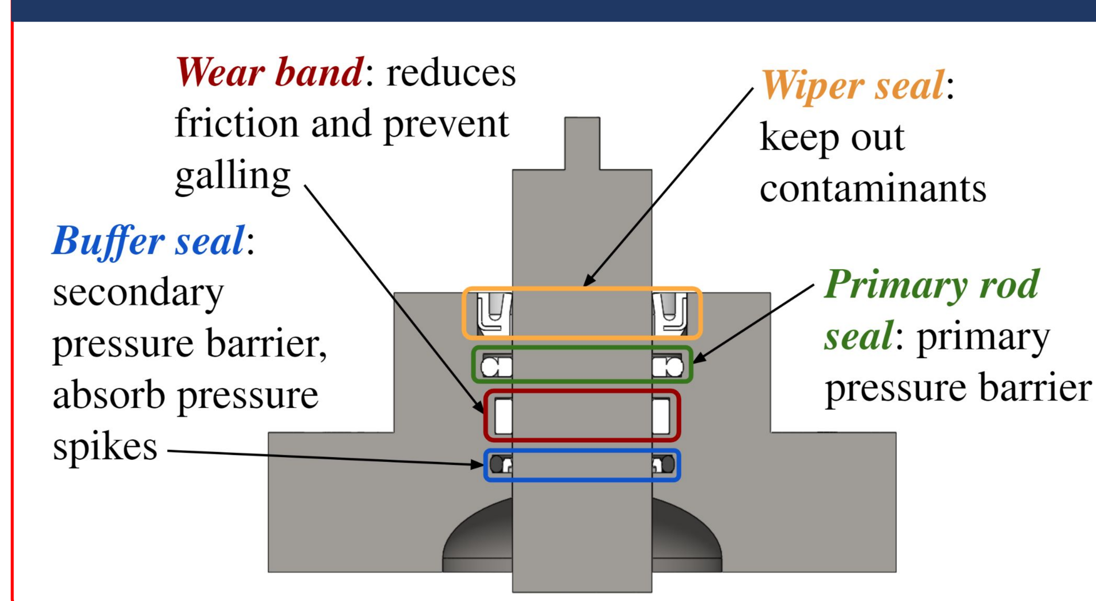
Pretension Torque

$$T = KF_i d = 43.6\,ftlb$$

Joint Separation Safety Factor

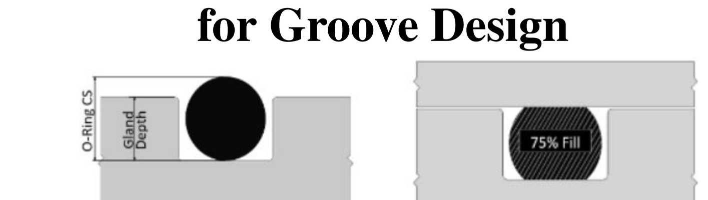
$$n_O = \frac{F_i}{P(1-C)} = 5.72$$

Seal Analysis



- Rod end seals used in hydraulic cylinders rated for 2300 psi
- Material selection: Bronze filled PTFE. Has self lubricating properties, applicable for dry conditions.

O-Ring Compression and Fill Ratio for Groove Design



Targeted *25% compression ratio* and *75% gland fill* for static face seal to design grooves with sufficient gland depth and width

Acknowledgements

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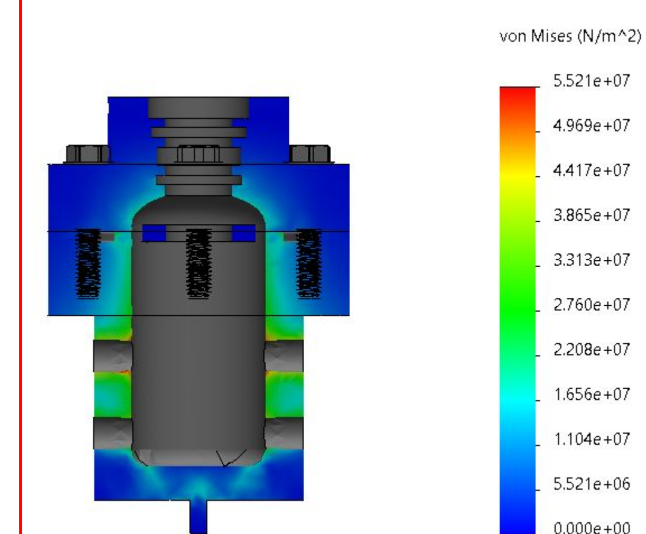
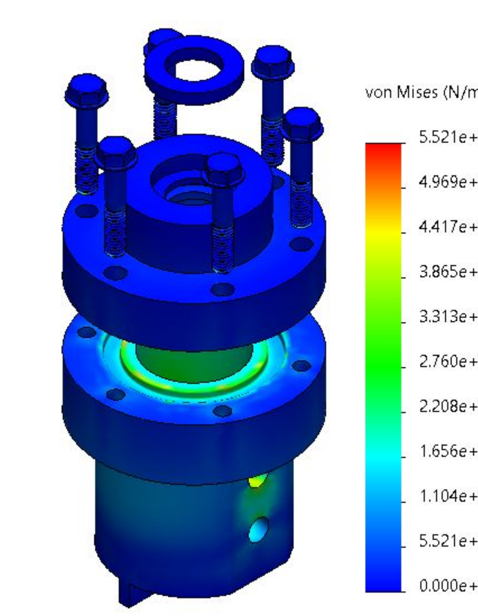
Design Validation

Pressure FEA

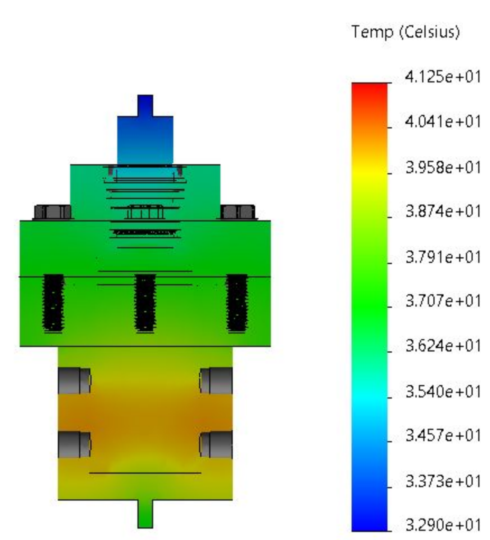


Stress distribution with 10 MPa (~1450 psi) internal load applied



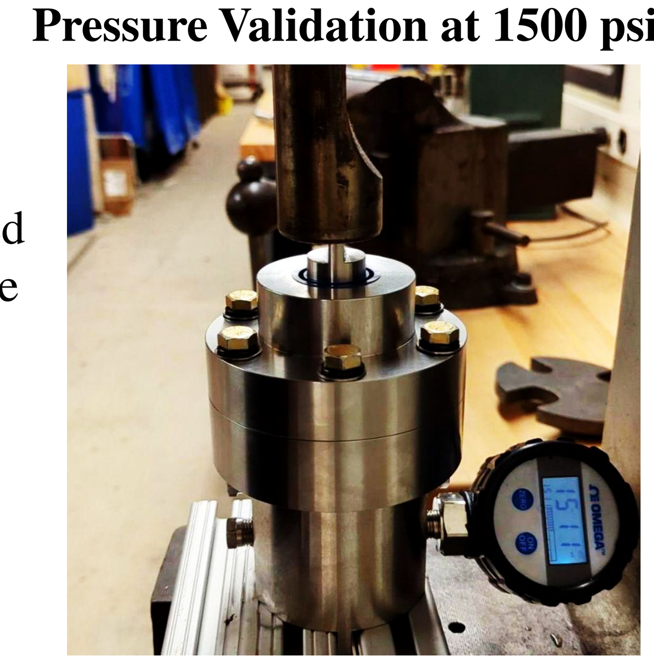
Max stress, located at the lid and body interface, is less than 7 MPa

Temperature FEA



Temperature distribution with 12 Watts applied to the sides and 25°C natural convection on all other faces

Pressure Validation at 1500 psi



Pressure test was conducted using press machine where pressure was applied and maintained at 1511 psi

Future Work / Exit Strategy

Future Work:

- Streamline temperature control, add backordered thermistor, and calibrate Arduino control
- Add and calibrate release valve spring
- Add filling valve so caps do not need frequent replacement

Exit Strategy:
Dr. Shefelbine’s lab will use our hand-off documents to finish the work listed above and conduct a full pressure and temperature test on the hydraulic Instron. From there, the vessel will be in her lab helping to grow cartilage cells!