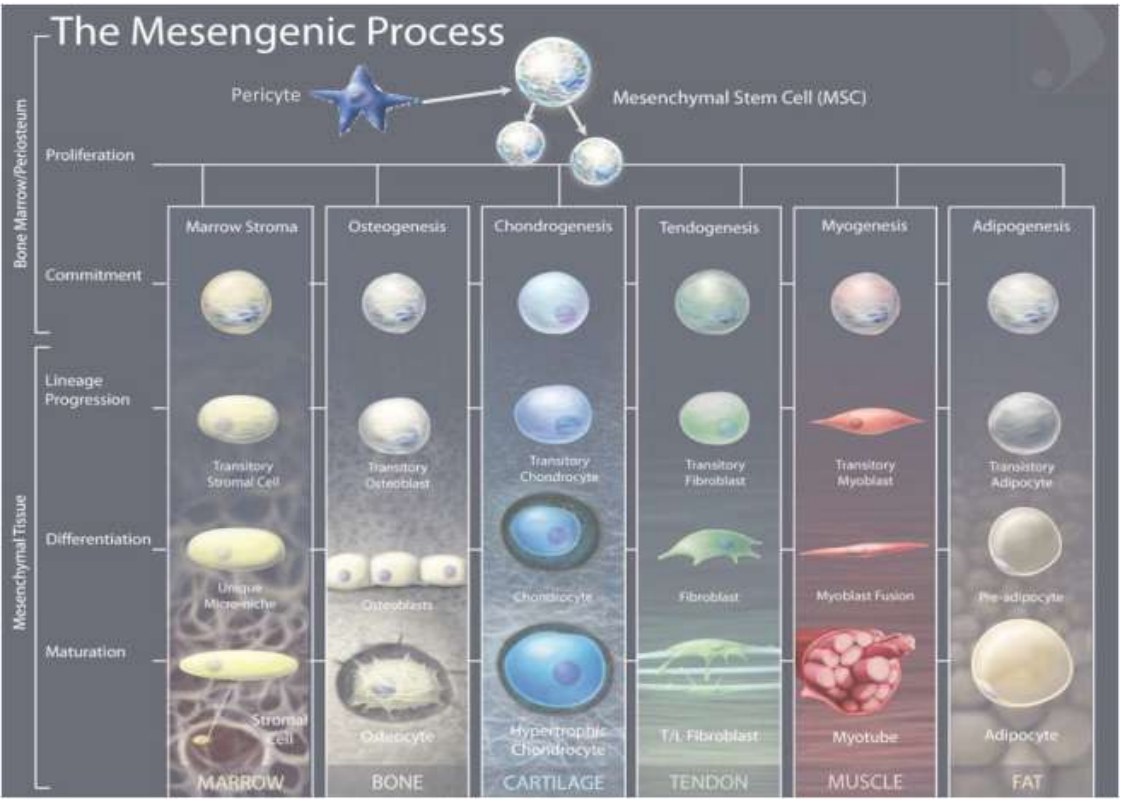
RUTGERS
THE STATE UNIVERSITY OF NEW JERSEY

NJCBM
NEW JERSEY CENTER FOR BIOMATERIALS

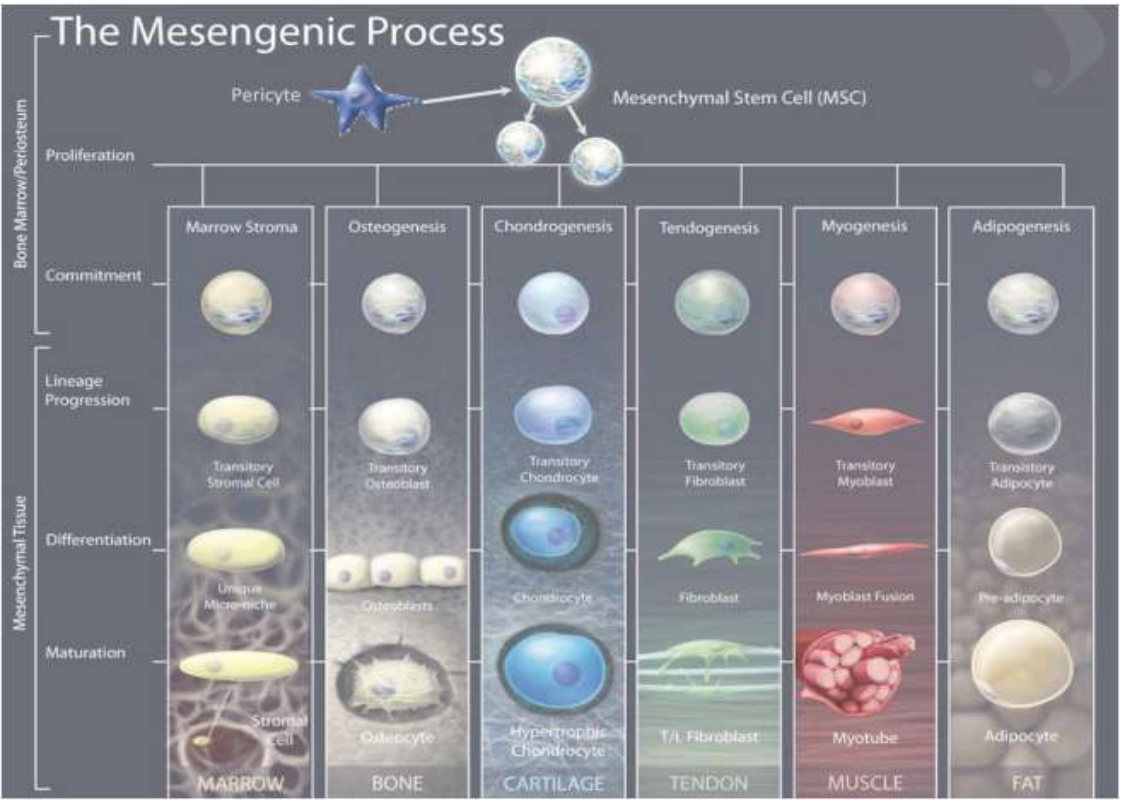
The 2016 Symposium on Biomaterials Science
October 24th to October 25th, 2016

Mesenchymal Stem Cell Response to Static Tension, Cyclic Tension, and Vibration

Brooke McClarren, Ayesha Aijaz, Matthew Teryek, Ronke Olabisi
Department of Biomedical Engineering, Rutgers University, New Brunswick, NJ



- Multipotent and capable of becoming any mesenchymal tissue.
- Certain stimuli can cause cell commitment.
  - Mechanical
  - Chemical
  - Electrical
  - Thermal



- Mechanical stimulation initiates differentiation down specific lineage
  - Substrate rigidity
  - Stress/Strain magnitude
  - Stress/Strain duration
  - Stress/Strain type:
  - shear, tension, compression,
  - Static vs cyclic

Mesenchymal Stem Cells (MSCs) in Tensile Strain

Load	Ref.	Cell	Scaffold	Parameter	Results
Static	1	hMSC	Collagen based	3% strain	osteogenic
	1	hMSC	Collagen based	10% strain	tenogenic
	2	mMSC	Poly(caprolactone)	10% strain	tenogenic
	3	gMSC	Poly(lactic-co-glycolic acid)	6.7 N	inhibition
	Static loading trends towards osteogenic lineages				
Cyclic	4	hMSC	Silicon, Gelatin 1%	10% strain	tenogenic
	5	hMSC	Silicon	8% strain	tenogenic
	5	hMSC	Silicon	2% strain	osteogenic
	Greater magnitude trends tenogenic. Lower magnitude trends to osteogenic.				

1. Chen et al. 2. Fang et al. 3. Van Eijk et al. 4. Zhang et al. 5. Jagodzinski et al.

MSCs in Compression, Shear, Vibration

Load	Ref.	Cell	Scaffold	Parameter	Results
Compressive	6	hMSC	Collagen Sponge	10% strain	osteogenesis
	6	hMSC	Collagen Sponge	15% strain	osteogenesis & chondrogenesis
	Investigated for chondrogenic differentiation. Small number result in osteogenesis				
Shear Stress	7	hMSC	2D construct	1.2 Pa	osteogenesis
	8	hMSC	Ficoll Paque	9 dynes/cm^2	osteogenesis
	Trends towards osteogenesis. Few cases, inhibition of osteogenesis.				
Vibration	9	hMSC	Microencapsulation	0.3 g	osteogenic

6. Michalopoulos et al. 7. Delaine-Smith et al. 8. Yourek et al. 9. Mehta et al.

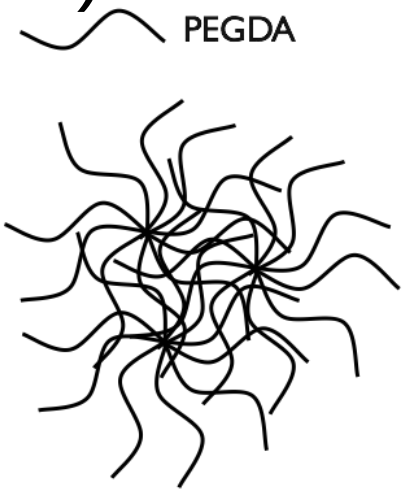
Scaffold Study Drawbacks

- Scaffolds were modified with biofactors
- Scaffolds were derived from natural sources
- Cells were seeded on scaffolds in 2D configurations

Scaffolds adds biological input and confounds the mechanical stimuli. In order to isolate the mechanical stimuli, it is necessary to use a bioinert scaffold.

Polyethylene glycol diacrylate (PEGDA)

- Widely used in tissue engineering
- Highly hydrophilic
- Crosslinked synthetic polymer-based networks
- Tunable physical properties
- Bioinert
- Resists protein adsorption
- Low cell adhesion (eg: immune cells)
- Lacks biochemical or microarchitectural cues

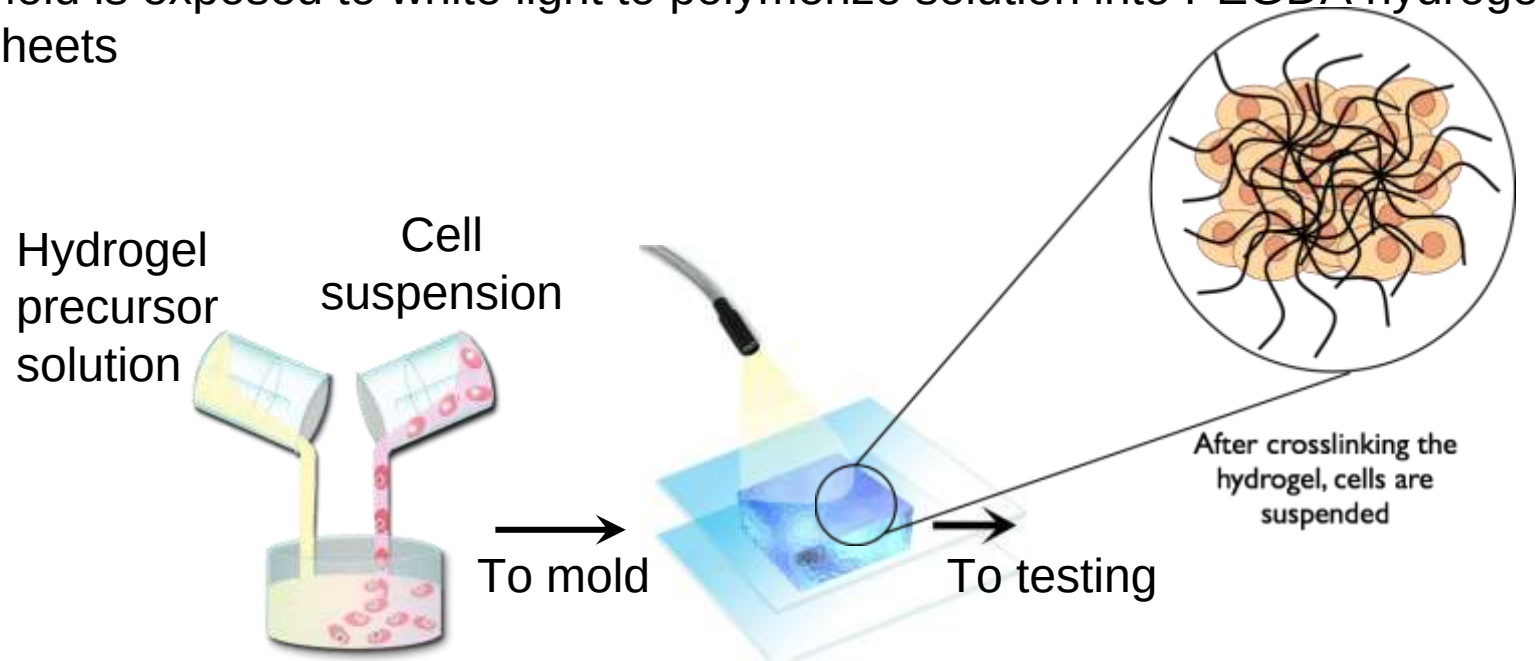


Crosslinked PEGDA comprises a PEGDA hydrogel

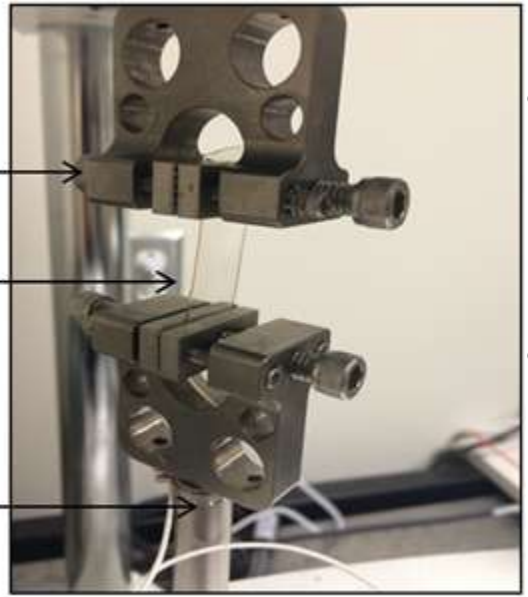
These combined properties enables the isolation of cell responses to mechanical stimulation within PEGDA scaffolds without confounding biochemical/micro-architectural cues imparted by natural polymers.

Cell Encapsulation

- Cell suspensions are combined with polymer precursors
- Cell-precursor solution is placed within a mold
- Mold is exposed to white light to polymerize solution into PEGDA hydrogel sheets

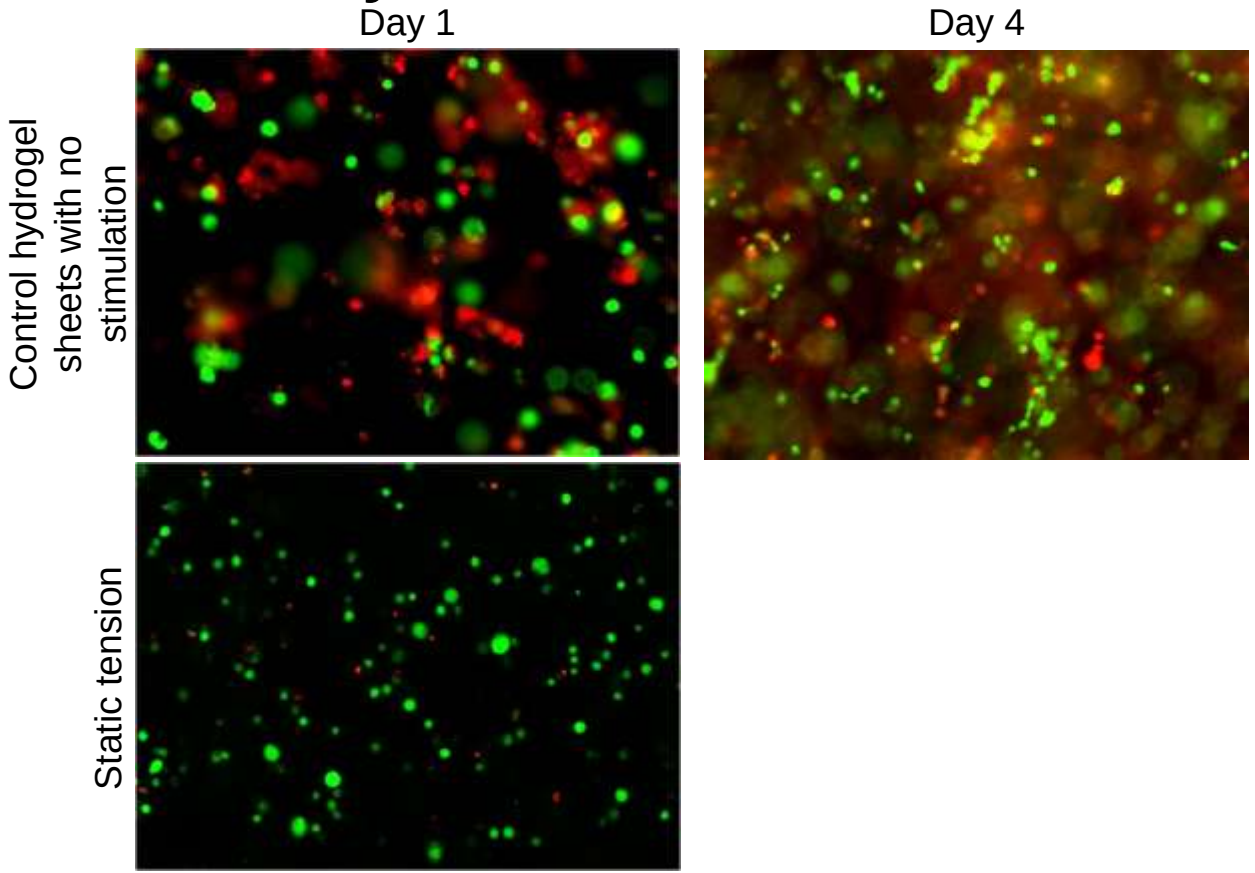


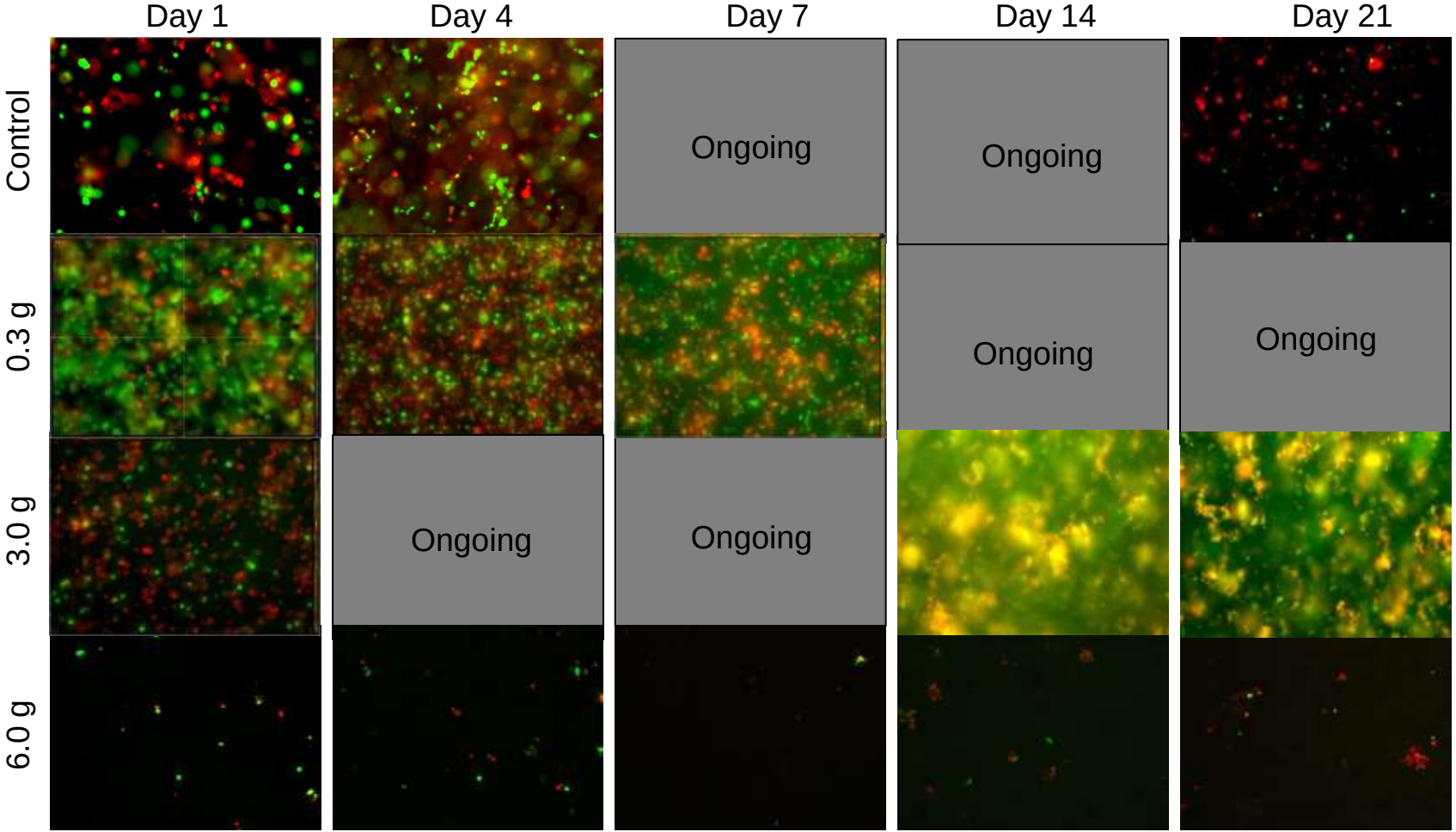
Tensile Loading



- Hydrogel sheets were suspended within plastic films to retain media.
- Sheets within films were subjected to 24 hr:
  - Static tension at 2 N
  - Cyclic tension at 2 N, 10 Hz
  - Vibration at 0.3 g, 3.0 g, 6.0 g
- Viability and differentiation were evaluated on Days 1, 4, 7, 14, and 21
  - Calcein AM, Ethidium Homodimer-1 (Live/Dead)
  - Alkaline Phosphatase (Osteogenesis)
  - Alizarin Red (Osteogenesis)
  - Oil Red O (Adipogenesis)

Results: Viability




Day 1
Day 4
Day 7
Day 14
Day 21
Control
0.3 g
3.0 g
6.0 g
Ongoing
Ongoing
Ongoing
Ongoing
Ongoing

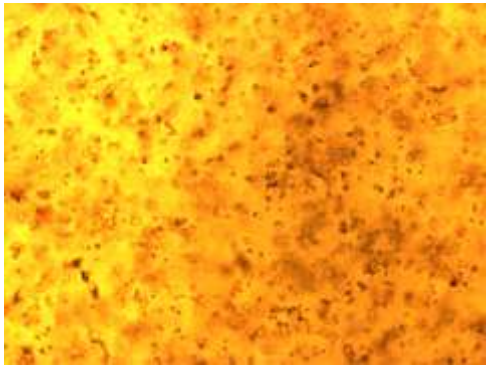
Results: Viability

Cell Viability from Day 1 to Day 21 of test samples with live (green) and dead (red) cells. The stained microspheres were then observed under an epifluorescent microscope.

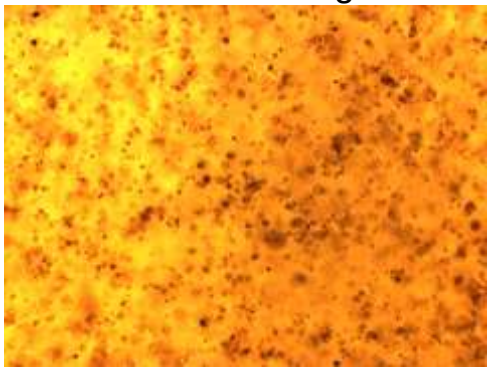
- Higher cell viability with mild vibration
- Lowered cell viability with high vibration
- Static tension higher viability than control
- Overall viability decreases over later time points

Results: Alkaline Phosphatase (Day 4)

Control



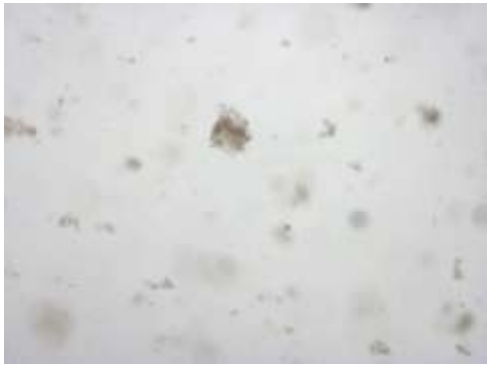
Vibration 0.3 g

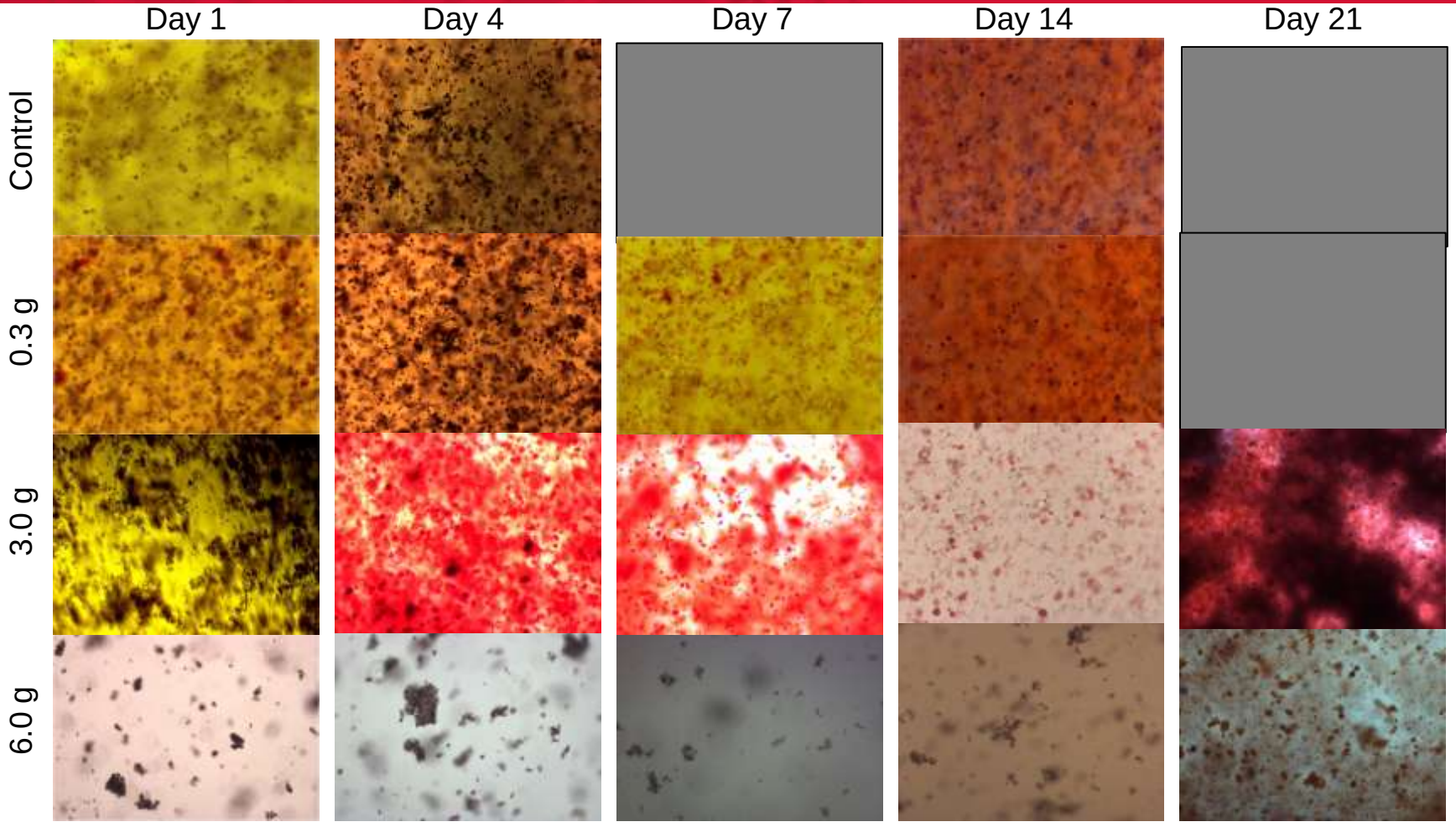


Vibration 3.0 g

Ongoing

Vibration 6.0 g

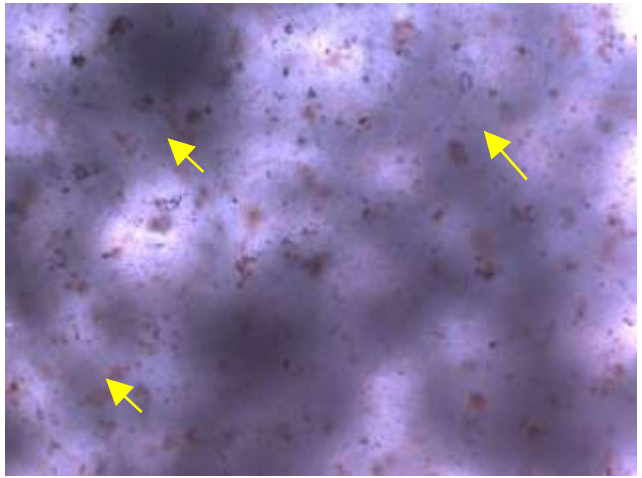



Day 1
Day 4
Day 7
Day 14
Day 21
Control
0.3 g
3.0 g
6.0 g

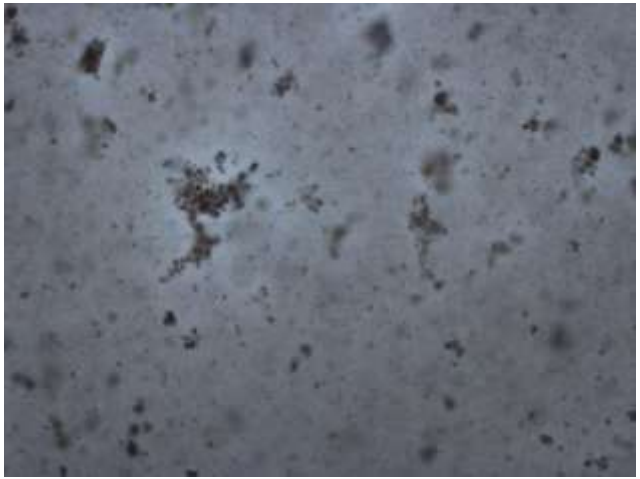
Results: Adipogenesis

Oil Red O stains for test samples on Day 21

Vibration 3.0 g



Vibration 6.0 g



Conclusions

- Mechanical stimuli of static tension, 0.3 g vibration, 3.0 g vibration improve viability of PEGDA hydrogel encapsulated cells.
- Vibrations of 6 g appear to cause aggregation of cells and reduce cell viability.
- Vibration of 0.3 g and 3 g highly promotes osteogenic differentiation.
- Vibration of 3.0 g promotes adipogenic differentiation.

Acknowledgements

Members of the Olabisi Lab
Kris White
Corina White
Sneha Mehta

The first author was supported by the following:
NASA Space Grant Consortium Academic Year Fellowship
NASA Space Grant Consortium Summer Fellowship
Rutgers Douglass Summer Stipend