

## Cellular Responses to External Mechanical Stimuli When Seeded to 3d Collagen

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**INTRODUCTION:** Collagen is a naturally occurring visco-elastic protein and widely used biomaterial in Tissue engineering. Mechanical stimulation of cell seeded collagen constructs and its effects on cell orientation, intracellular signalling and molecular responses have been reported in literature<sup>2</sup>. Monitoring of cellular responses to mechanical stimulation include synthesis of active regulatory molecules such as growth factors or hormones, changes in matrix synthesis, cell alignment and enzyme release. The aim of this study was to investigate cellular responses to pre strained, stiffer and more organised collagen bio-artificial matrices.

**METHODS:** Human Dermal Fibroblast (HDF) as well as Neonatal Human Dermal Fibroblasts (NHDF) cells seeded (1million/ml) collagen constructs were subjected to 0%, 5% and 10% pre-strain using a computer driven tensional loading device (t-CFM) capable of unidirectional loading. force<sup>1</sup> generated by the cells monitored for 24 hours. Furthermore, cells were Fetal Calf Serum (FCS) starved for 1 hour post strain, to stop/control cell attachment and spreading. FCS was then added, at 1 hour, and contraction force was again monitored for 24 hours.

**RESULTS:** Results showed significant reduction on the contraction force generated by the cells when constructs were pre strained (5% and 10%) compared to non pre-strained (0%). FCS starvation for 1 hour did not alter this effect (Figure 1). However it did introduce a more rapid contraction slope. Furthermore, contraction force generation was increasingly delayed as the pre strain increased and delayed even further when constructs were FCS starved.

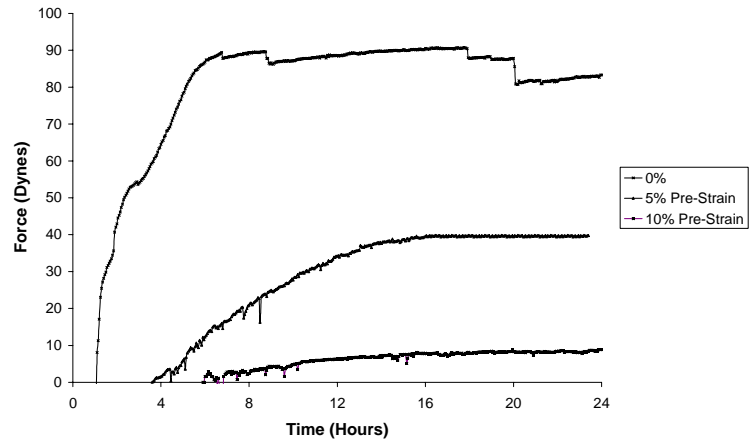


Figure 1. HNFF's contraction profile following pre strain and 1h FCS starvation

**DISCUSSION & CONCLUSIONS:** The increased stiffness of a Tissue Engineered construct by means of external mechanical stimuli will have to be tailored to account to elicit predictable cellular responses. Furthermore, FCS cell starvation will have to be taken into account on rate as well as initiation time of cellular contractile forces.

### REFERENCES:

<sup>1</sup>M.Eastwood,V.C.Mudera,D.A.McGrouther,R.A.Brown (1998) Effect of precise mechanical loading on fibroblast populated collagen lattices: Morphological changes. *Cell motility and the cytoskeleton* **40**:13-21

<sup>2</sup>V.C.Mudera,R.Pleass,M.Eastwood,R.Tarnuzzer,G.Schultz,P.Khaw,D.A.McGrouther,R.A.Brown (2000) Molecular responses of human dermal fibroblasts to dual cues:Contact guidance and mechanical load.*Cell motility and the cytoskeleton* **45**:1-9

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