

## Contractile Properties of fibroblasts derived from Primary frozen shoulder and effects of TGF beta 1 stimulation

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**INTRODUCTION:** Primary Frozen Shoulder (PFS) is a debilitating disease of unknown aetiology. There is fibrosis and contracture of the coracohumeral ligament, tissues of the rotator interval and the glenohumeral ligaments, leading to restrictive shoulder movements requiring surgical intervention [1]. Frozen shoulder has been postulated to be Dupuytren's disease of the shoulder with an association inferred since 1936. The purpose of the study was to test the hypothesis that cellular mechanisms of fibroblasts derived from primary frozen shoulder exhibited similar activity in terms of contraction and response to cytokine (transforming growth factor beta1) to fibroblasts derived from Dupuytren's disease. Understanding of cellular responses is critical to developing non surgical treatment strategies.

**METHODS:** Primary explant cultures of fibroblasts from six patients with PFS and four control patients were obtained using standard tissue culture techniques. Fibroblasts were seeded in 3-D collagen constructs and contraction force generated over 24hours measured using a culture force monitor (CFM) in real time. Increasing concentrations of TGF-beta1 were added to cell seeded gels and force generated measured using the CFM over 24hours. These mechanical output data were statistically compared to data available from Dupuytren's disease.

**RESULTS:** Compared to Dupuytren's fibroblasts [2], PFS fibroblasts showed a statistically reduced ability to contract a 3-D collagen gel over 24hours ( $p < 0.01$ ). In Dupuytren's disease, fibroblasts derived from nodules and cords generate peak forces of 140dynes and 110dynes respectively, while PFS fibroblasts generated peak force of 8dynes. The response to TGF-beta1 stimulation, which has been shown to enhance peak force contraction in Dupuytren's fibroblasts had no effect on PFS fibroblasts and this was statistically significant ( $p < 0.01$ ).

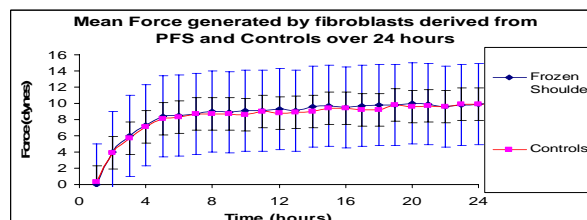


Fig. 1: Contraction Profiles of fibroblasts derived from primary frozen shoulder (n=6) as compared to control derived fibroblasts (n=4)

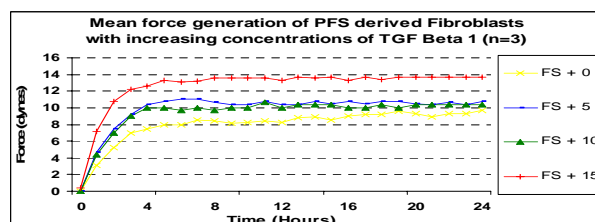


Fig. 1: Contraction Profiles of PFS derived fibroblasts (n=3) to increasing concentrations of TGF beta 1 (0, 5, 10 & 15ng/ml)

**DISCUSSION & CONCLUSIONS:** These data suggest intrinsic differences in cellular activity and mechanisms between Dupuytren's and Primary Frozen Shoulder even though clinically they both manifest with a contracted extracellular matrix affecting function and requiring surgical intervention. This may explain increasing post surgically recurrence in Dupuytren's as compared to Primary Frozen Shoulder release.

### REFERENCES:

- <sup>1</sup> Ozaki J *et al* (1989) *JBJS* **71A**:1511-1515
- <sup>2</sup> Bisson M *et al* (2004) *PRS* **113(2)**:611-620

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