Biocompatibility of the Subacromial Balloon Spacer: an *in vivo* Murine Pouch Model Cytokine Analysis

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INTRODUCTION: There are several methods of treating massive rotator cuff tears in patients without severe glenohumeral arthritis. Subacromial balloon spacers have emerged as one solution to this problem. Previous studies identified a lasting film in the subacromial space well after the balloon should have dissolved, and there is limited information regarding the biocompatibility and reactivity of the resorbable implant. This study sought to characterize the inflammatory response to the balloons histologically and via cytokine production using an established *in-vivo* animal model.

METHODS: Forty-two BALB/c mice were randomized into two groups: control (no balloon device, n=4/time point) and experimental (balloon device implanted, n=10/time point). Time points were 1, 4, and 12 weeks creating 3 subgroups that contained 4 controls and 10 experimental mice. One balloon subacromial spacer was sectioned into equally sized 3mm diameter sections. Subcutaneous mouse air pouches were created and one 3mm diameter sample was implanted into each mouse pouch. No implants were placed in control pouches. Sacrifice occurred at the noted timepoints. Bead array assay was used to measure cytokines TGF-B1, IL-13, IL-1B, IL-4, IL-6, IL-10, and TNF-α. Histologic analysis was also performed for hematoxylin and eosin (H&E) stained sections.

RESULTS:

Cytokine analysis: Cytokines analysis curves correlated appropriately to the array standards. At 1 week and 4 weeks, all cytokines besides TGF-B1 remained within the standard curve and were therefore undetectable. At 12 weeks all cytokines were undetectable (Table 1).

Histologic analysis: No differences were seen between the control and experimental groups histologically. When characterizing the pouch histology: At 1 week, pouch membranes were dense and infiltrated with inflammatory neutrophils and few macrophages. At 4 weeks the membranes were less densely populated with cells, consisting of mostly fibroblasts, few neutrophils, and no macrophages or lymphocytes. At 12 weeks, the pouch membranes had few cell layers showing mostly fibroblasts.

DISCUSSION AND CONCLUSION:

Inflammatory cytokines were well below the detectable limit, and the inflammatory profile of the subacromial balloon spacer based on histologic analysis was quite benign in an *in-vivo* animal model. Histologic response was similar between the balloons and controls. While a thin film may remain after resorption of balloons clinically, the inflammatory response appeared minimal. Further studies using human subjects and/or insufflated balloons may be helpful in better defining the biocompatibility profile of subacromial balloon spacers.

Table 1: Average concentration of experimental and control group cytokines in picogram per milliliter (pg/ml) at 1, 4, and 12 weeks

Group 1 (1 week)				
Cytokine	R^2	LOD (pg/ml)	Experimental Group (pg/ml)	Control Group (pg/ml)
IL-1B	0.992	7.28	3.37	3.44
IL-6*	0.985	11.95	1.93	1.53
TNF-α	0.990	14.79	1.96	2.06
IL-10*	0.992	27.51	8.48	9.35
TGF-B1*	0.983	23.40	26.34	24.69
IL-4	0.987	13.36	2.56	2.58
IL-13	0.971	27.69	2.64	2.86
Group 2 (4 weeks)				
Cytokine	R^2	LOD (pg/ml)	Experimental Group (pg/ml)	Control Group (pg/ml)
IL-1B	0.992	11.41	1.50	0.88
IL-6*	0.986	10.86	0.47	0.10
TNF-α	0.990	7.67	0.77	0.32
IL-10*	0.992	19.17	4.75	2.05
TGF-B1*	0.983	10.65	19.40	0.77
IL-4	0.988	10.99	0.85	0.30
IL-13	0.972	8.59	1.25	0.29
Group 3 (12 weeks)				
Cytokine	R^2	LOD (pg/ml)	Experimental Group (pg/ml)	Control Group (pg/ml)
IL-1B	0.992	11.32	2.53	1.73
IL-6*	0.986	9.08	0.23	0.01
TNF-α	0.990	5.81	0.18	0.08
IL-10*	0.992	32.12	3.49	2.25
TGF-B1*	0.970	62.52	11.50	5.44
IL-4	0.987	12.27	0.31	0.23
IL-13	0.973	12.27	0.34	0.13

LOD = Level of Detection

*Indicates growth factor or cytokine that promotes tissue repair as a growth factor or by inhibiting inflammation