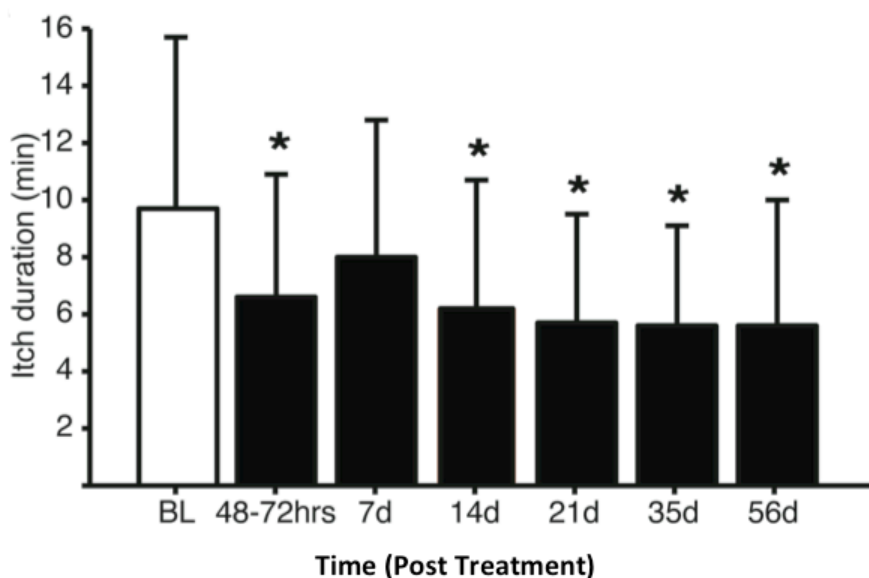


## Supplementary Material

### Results:

#### A. Itch Duration:

**Figure S1: Histamine-induced itch duration following cryolipolysis.** Data shown as mean (SD). P-values determined using mixed model repeated measures ANOVA with Bonferroni correction. Asterisks indicate level of significance compared to baseline. \*,  $p < 0.05$ .



**Table S1** shows histamine-induced itch duration data for the treated and control sides at each time point. Pair-wise comparisons were performed to assess the itch duration in (1) cryolipolysis treatment vs control side at each time point, and (2) post-treatment data vs baseline (for treated site, as well as control site).

For treated vs control analysis, there were no significant differences in itch duration at any time point. At the treated side, post-treatment itch duration was significantly decreased at 48-72hr, and between Days 14 to 56 when compared to baseline. At the control side, post-treatment itch duration was significantly decreased at all time points when compared to baseline.

**Table S1: Histamine-induced itch duration (min) in the control and cryolipolysis treated areas<sup>A</sup>.**

Time	Pairwise Comparisons				
	Control	Treatment	Side	Time	
			Tx vs. Control	Control: vs BL	Tx.: vs. BL
<i>Baseline</i>	10.2 (7.3-13.2)	9.7 (6.8-12.7)	0.639	-	-
<i>48-72h</i>	7.5 (4.6-10.5)	6.6 (3.7-9.6)	0.435	<b>0.009*</b>	<b>0.02*</b>
<i>Day 7</i>	7.1 (4.1-10.1)	8.0 (5.0-11.0)	0.461	0.154	<b>0.009*</b>
<i>Day 14</i>	6.0 (3.1-8.9)	6.2 (3.2-9.2)	0.874	<b>0.004*</b>	<b>&lt;0.001*</b>
<i>Day 21</i>	5.7 (2.8-8.7)	5.7 (2.8-8.7)	1	<b>&lt;0.001*</b>	<b>&lt;0.001*</b>
<i>Day 35</i>	5.1 (2.1-8.0)	5.6 (2.7-8.6)	0.639	<b>&lt;0.001*</b>	<b>&lt;0.001*</b>
<i>Day 56</i>	5.4 (2.4-8.3)	5.6 (2.7-8.6)	0.815	<b>&lt;0.001*</b>	<b>&lt;0.001*</b>

A. Mean (95% Confidence Interval); p values determined from Mixed Model Repeated Measures ANOVA with Bonferroni correction (assuming significance at  $p < 0.05$ ).

\* Indicates statistically significant differences

**B. Itch intensity:** Table S2 shows histamine-induced itch intensity data for the treated and control sides at each time point. Pair-wise comparisons were performed to assess the itch intensity in (1) cryolipolysis treatment vs control side at each time point, and (2) post-treatment data vs baseline (for treated site, as well as control site). There are no significant differences in mean itch intensity at the treated side or at the control side following histamine-iontophoresis. There are no differences in itch intensity between control and treated sides at each time point.

**Table S2: Histamine-induced mean itch intensity in the control and cryolipolysis treated areas<sup>A</sup>.**

Time	Pairwise Comparisons				
	Control	Treatment	Side	Time	
			Tx vs. Control	Control: vs BL	Tx.: vs. BL
<i>Baseline</i>	2.0 (1.0-3.0)	1.9 (1.0-2.9)	0.92	-	-
<i>48-72h</i>	2.2 (1.2-3.2)	1.8 (0.8-2.8)	0.45	0.71	0.76
<i>Day 7</i>	1.6 (0.7-2.6)	2.3 (1.4-3.3)	0.21	0.51	0.48
<i>Day 14</i>	1.5 (0.6-2.5)	2.0 (1.0-3.0)	0.38	0.51	0.92
<i>Day 21</i>	1.7 (0.7-2.7)	1.5 (0.5-2.5)	0.71	0.38	0.40
<i>Day 35</i>	1.2 (0.2-2.2)	1.6 (0.7-2.6)	0.42	0.13	0.55
<i>Day 56</i>	1.4 (0.4-2.4)	1.5 (0.5-2.5)	0.87	0.28	0.42

A. Mean (95% Confidence Interval); p values determined from Mixed Model Repeated Measures ANOVA with Bonferroni correction (assuming significance at  $p < 0.05$ ).

**Table S3: Histamine-induced peak itch intensity in the control and cryolipolysis treated areas<sup>A</sup>.**

Time	Pairwise Comparisons				
	Control	Treatment	Side	Time	
			Tx vs. Control	Control: vs BL	Tx.: vs. BL
<i>Baseline</i>	6.0 (4.0-8.0)	5.2 (3.2-7.1)	0.10	-	-
<i>48-72h</i>	5.7 (3.8-7.7)	6.0 (4.0-8.0)	0.58	0.58	0.10
<i>Day 7</i>	5.1 (3.1-7.1)	5.9 (3.9-7.9)	0.13	0.08	0.16
<i>Day 14</i>	5.3 (3.3-7.2)	6.2 (4.2-8.1)	0.07	0.14	<b>0.05*</b>
<i>Day 21</i>	5.6 (3.7-7.6)	5.6 (3.6-7.6)	1.00	0.46	0.36
<i>Day 35</i>	5.1 (3.1-7.1)	5.3 (3.3-7.2)	0.71	0.07	0.85
<i>Day 56</i>	4.6 (2.7-6.6)	5.1 (3.1-7.1)	0.36	<b>0.01*</b>	0.85

A. Mean (95% Confidence Interval); p values determined from Mixed Model Repeated Measures ANOVA with Bonferroni correction (assuming significance at  $p < 0.05$ ).

\* Indicates statistically significant differences

### C. Wheal and flare reaction:

Erythema (flare) and wheal diameter at 10 minutes after histamine iontophoresis were measured at each time point. **Table S4** shows histamine-induced erythema (flare) diameter was significantly smaller in the treated flank at 48-72 hrs, Days 7-, 21-, and 35- when compared to the control side. At the treated side, histamine-induced erythema diameter was significantly decreased at Days 7, 21 and 35 when compared to baseline. At the control side, histamine-induced erythema diameter was significantly decreased from Day 14 to Day 56 when compared to baseline. There were no significant differences in the wheal size at each time point (data not shown).

**Table S4: Histamine-induced erythema diameter (cm) in the control and cryolipolysis treated areas<sup>A</sup>.**

Time			Side	Time	Time
	Control	Treatment	Tx vs. Control	Control vs BL	Tx vs. BL
<i>Baseline</i>	9.2 (7.9-10.6)	8.5 (7.2-9.9)	0.12	-	-
<i>48-72h</i>	8.9 (7.5-10.3)	7.6 (6.2-9.0)	<b>0.014*</b>	0.52	0.09
<i>Day 7</i>	8.6 (7.2 -10.0)	6.7 (5.3-8.2)	<b>&lt;0.001*</b>	0.21	<b>0.001*</b>
<i>Day 14</i>	8.2 (6.8-9.5)	7.6 (6.3-9.0)	0.26	<b>0.03*</b>	0.07
<i>Day 21</i>	8.3 (6.9-9.6)	7.0 (5.7-8.4)	<b>0.011*</b>	<b>0.047*</b>	<b>0.002*</b>
<i>Day 35</i>	8.1 (6.8-9.5)	7.2 (5.8-8.5)	<b>0.048*</b>	<b>0.024*</b>	<b>0.006*</b>
<i>Day 56</i>	7.9 (6.5-9.2)	7.6 (6.3-9.0)	0.64	<b>0.005*</b>	0.07

A. .Mean (95% Confidence Interval); p values determined from Mixed Model Repeated Measures ANOVA with Bonferroni correction (assuming significance at p<0.05).

\* Indicates statistically significant differences