Vibrating Needle During Venipuncture Reduces Insertion Force and Yields Lower and Less Variable Average Corticosterone Levels in Rodents

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Support

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Animal Research Needs

- Animal Research Needs
  - Described in the 2009 SBIR Omnibus Solicitation of the National Institutes of Health, Division of Aging Biology.
    - *Development of minimally-perturbing techniques for collecting blood from mice, rats, and other animals several times a day in sufficient quantities for measurement of hormone levels and other circulating factors in you*
  - The 3 R's: Reduction, Refinement, Replacement
    - *Less stressful sampling (Refinement)*
    - *Less variability = less animals (Reduction)*

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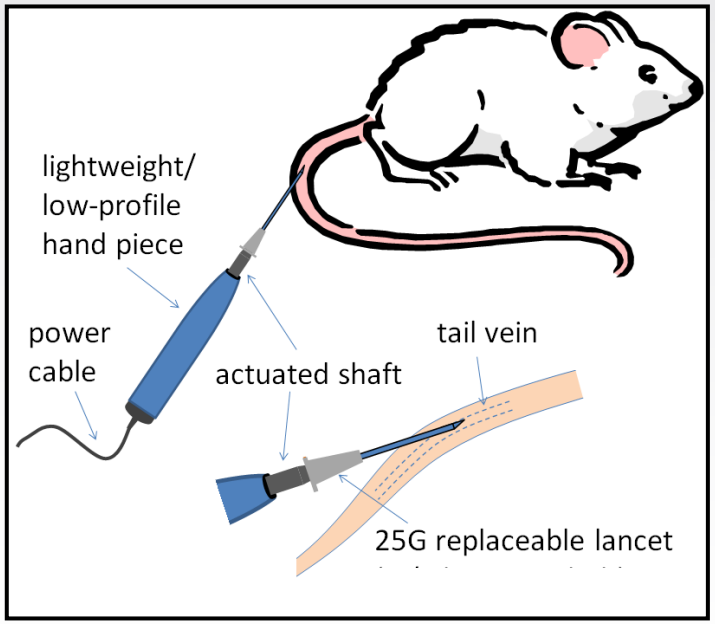
Basis of Approach

- Premise of the Solution: Vibration.
  - Gate Theory of Pain – describes anesthetic effect of vibration.
  - Mosquitos – drawing blood in nature.



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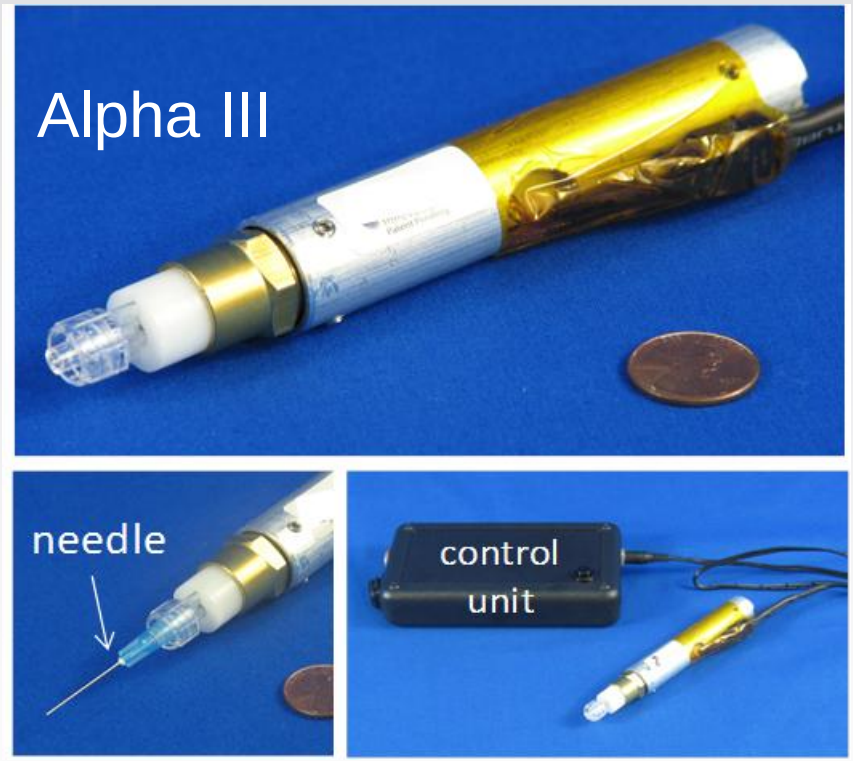
Proposed Solution

Vibrating Needle for Venipuncture, GentleSharp



Phase I SBIR Hypothesis:

+ An actuated resonance-assisted lancet introduction device will significantly reduce insertion force (>50%), leading to less stressful blood sampling in rodents, without causing additional tissue damage.

+ The hypothesis was tested in a serial blood sampling study with Sprague Dawley Rats.

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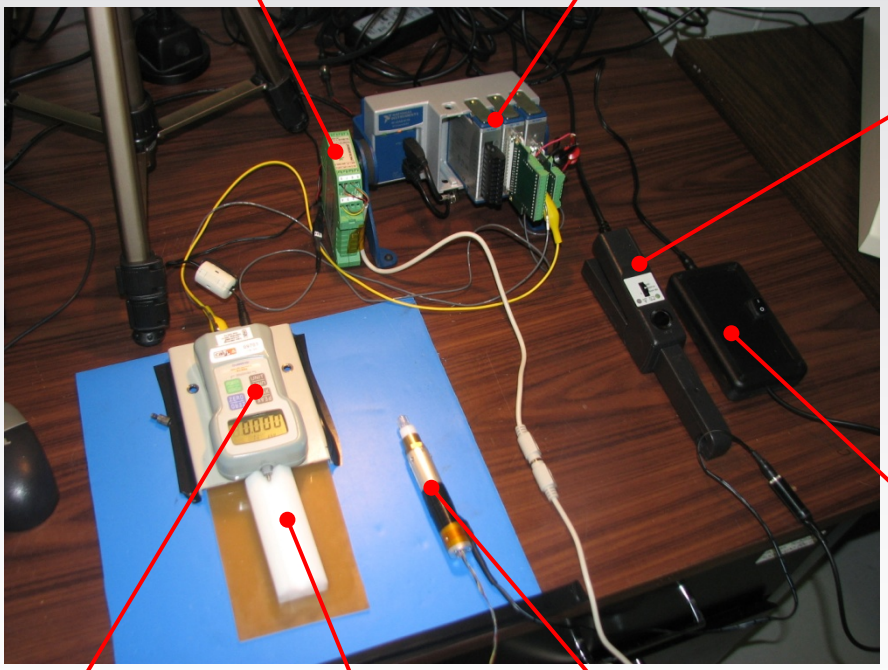
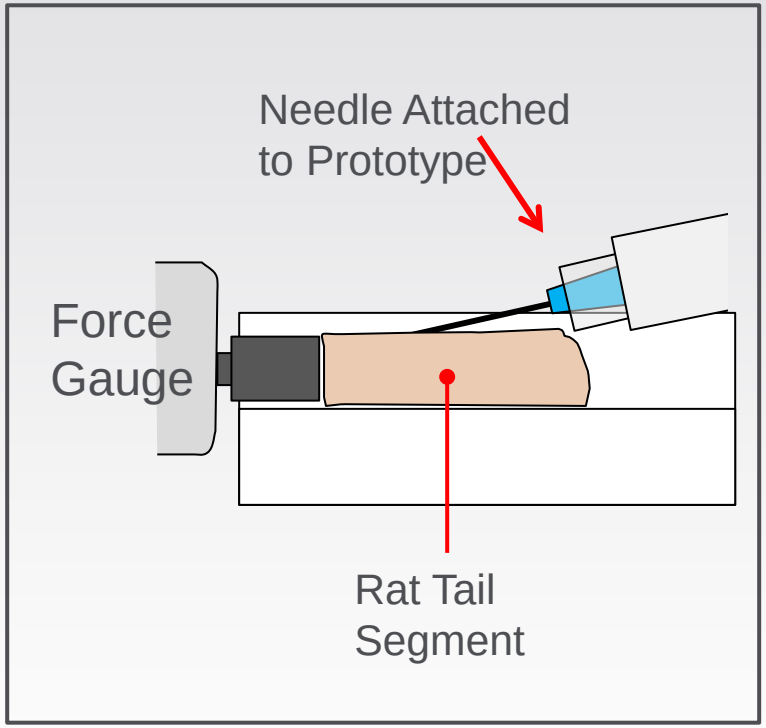
In vitro Testing, Cadaver Rat Tails

Insertion Force Measurement Set-up





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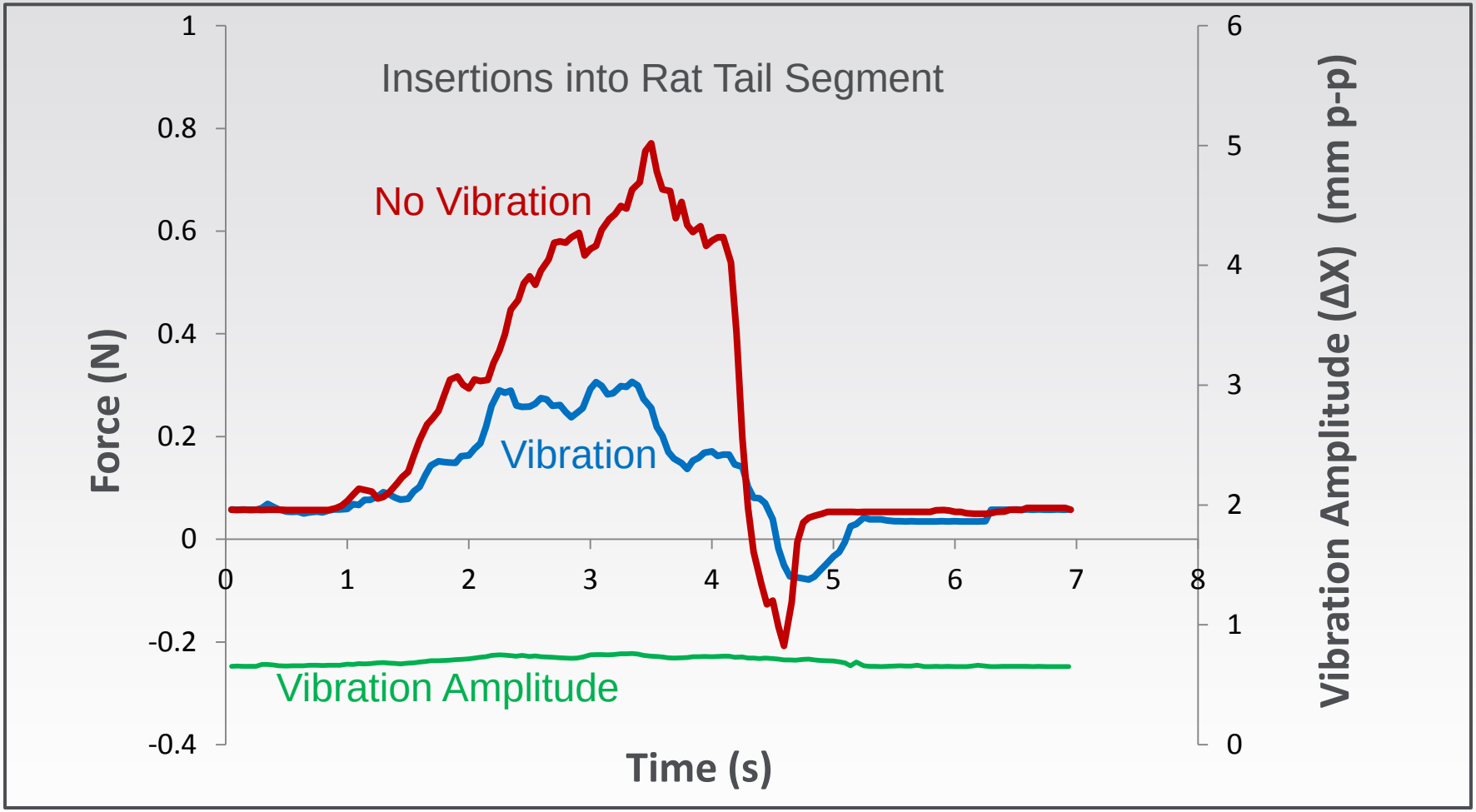
In vitro Insertion Force vs. Time Plots

Vibrated Needle Exhibits Lower Insertion Force



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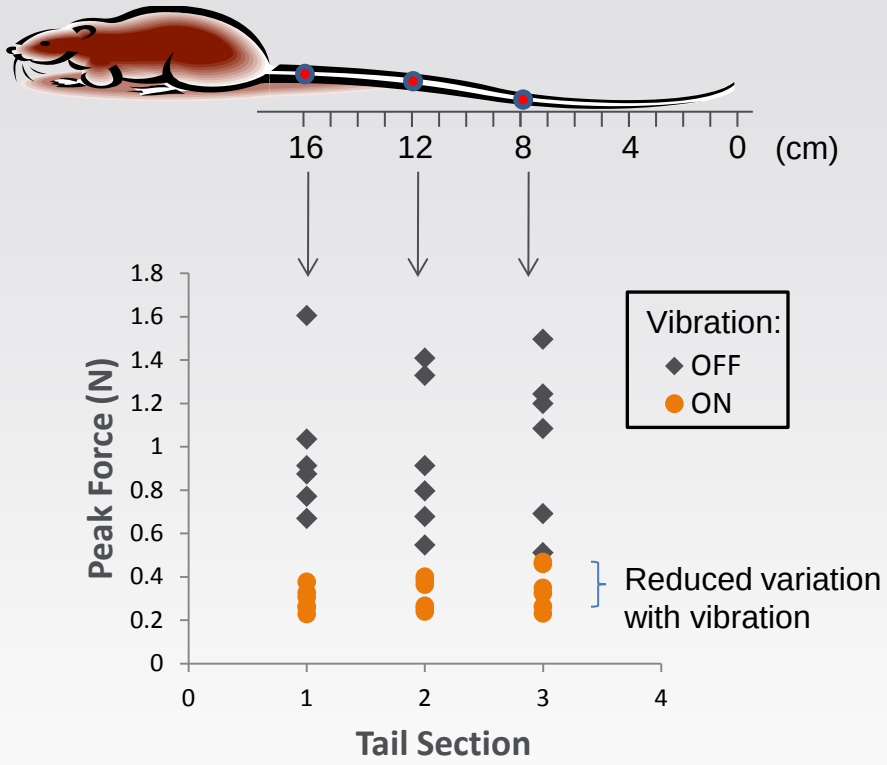
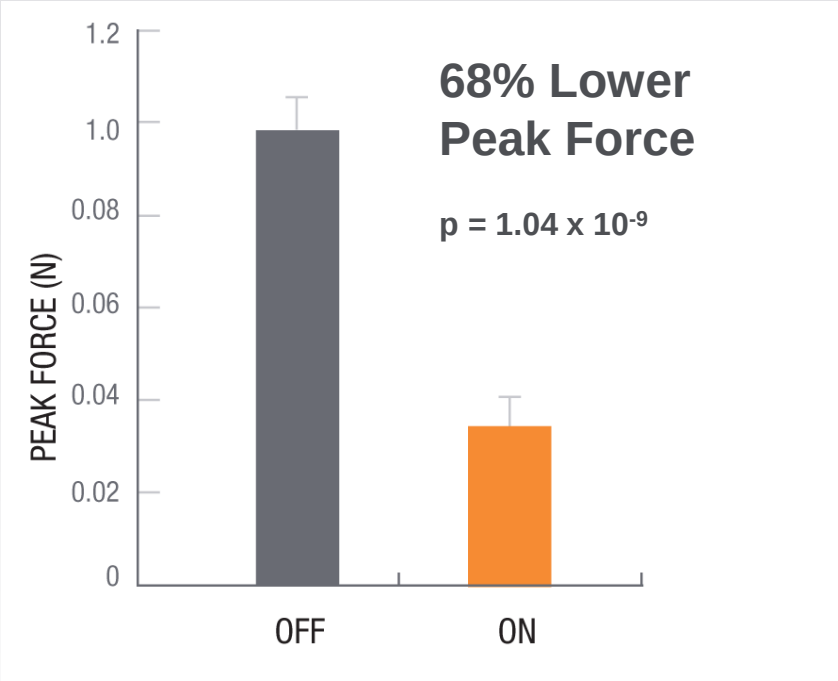
In vitro Peak Insertion Force Comparison

Vibrated Needle Exhibits Lower Peak Force





+ Testing performed on 6 rat tails at three locations.

+ N = 18 on/18 off.
+ Error bars = standard deviation.

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In vivo Serial Blood Sampling Experiment

Sprague Dawley Rat Study, Tail Site

- Research was conducted under an IACUC approved protocol in the Department of Nutritional Sciences, the Pennsylvania State University.
- PI: Dr. E. Unger (Phase I SBIR).

- Groups
  - Treatment (on): 10 subjects.
  - Control (off): 9 subjects.
- Protocol
  - Sample days occurred 3x at 1 week intervals.
  - 3 blood samples attempted in each rat on each sample day (each sample separated by ~1 hr).
- Data
  - Corticosterone concentration.
  - Number of attempts required for each sample (success/failure).
  - Vocalization/Movement (Likert).
  - Presence/absence of hematoma.

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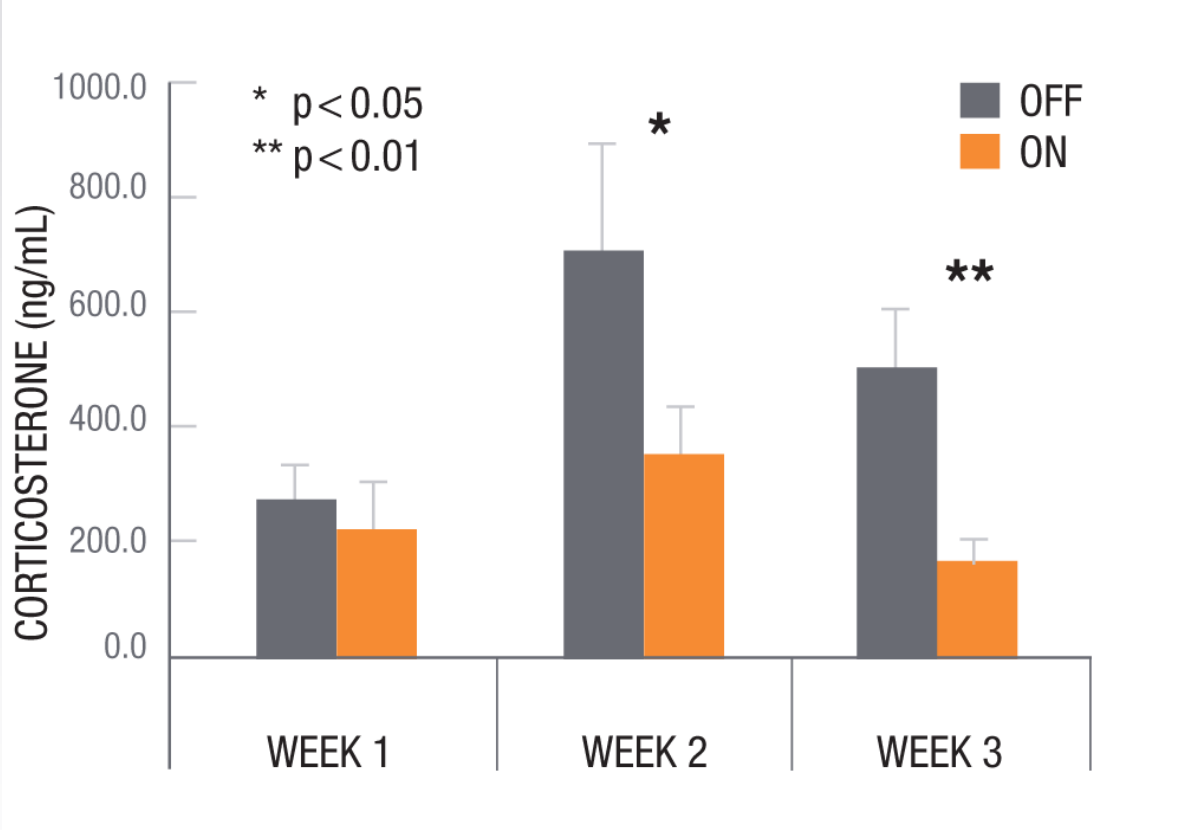
Stress Hormone Concentration Comparison

Subjects with Vibrated Needle Exhibit Lower Cort. Levels



Difference:	**9.7%**	**49.2%**	**65.2%**

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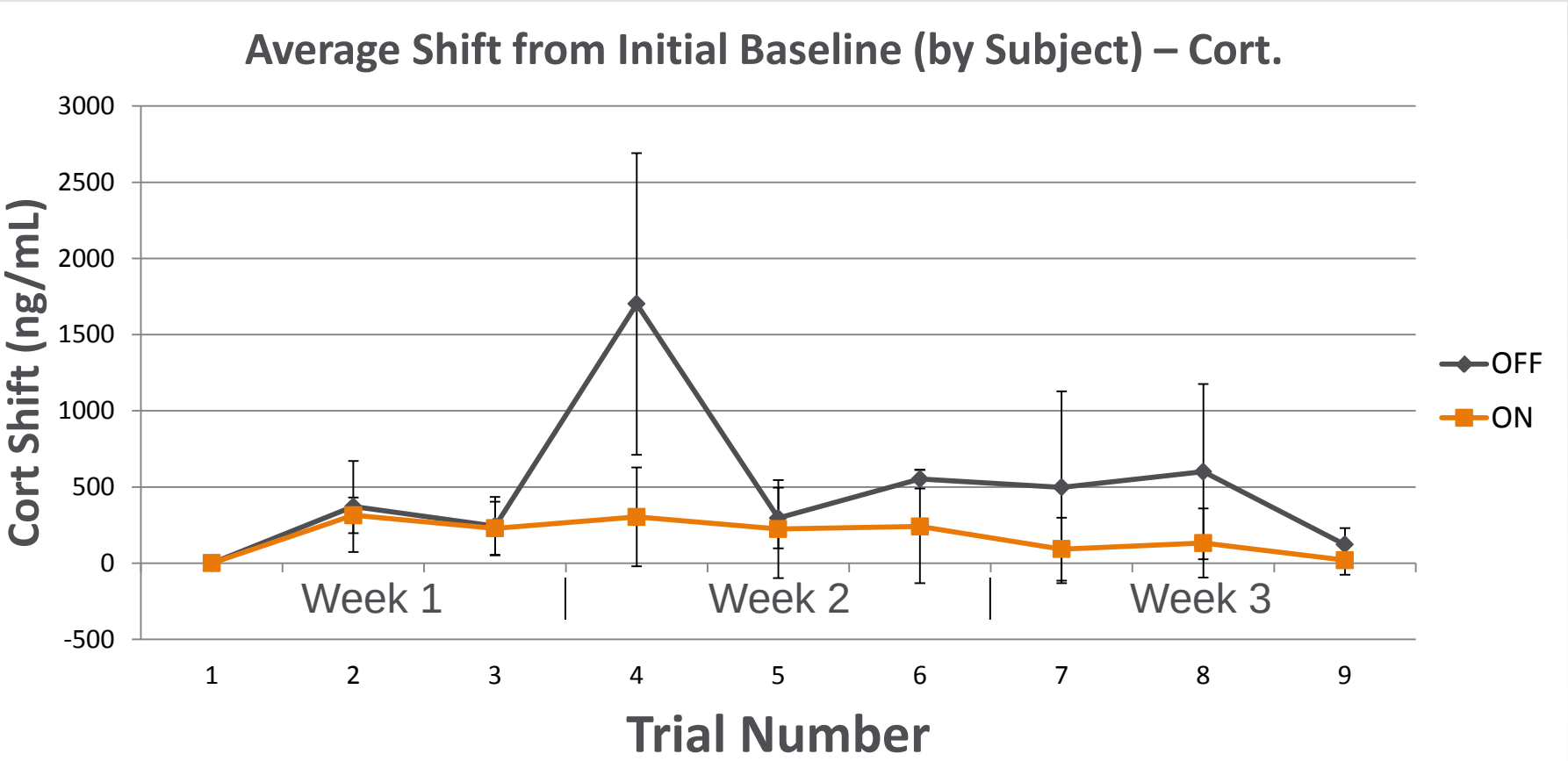
Over Study Duration Stress Hormone Comparison

Subjects with Vibrated Needle Exhibit Less Cort. Variation



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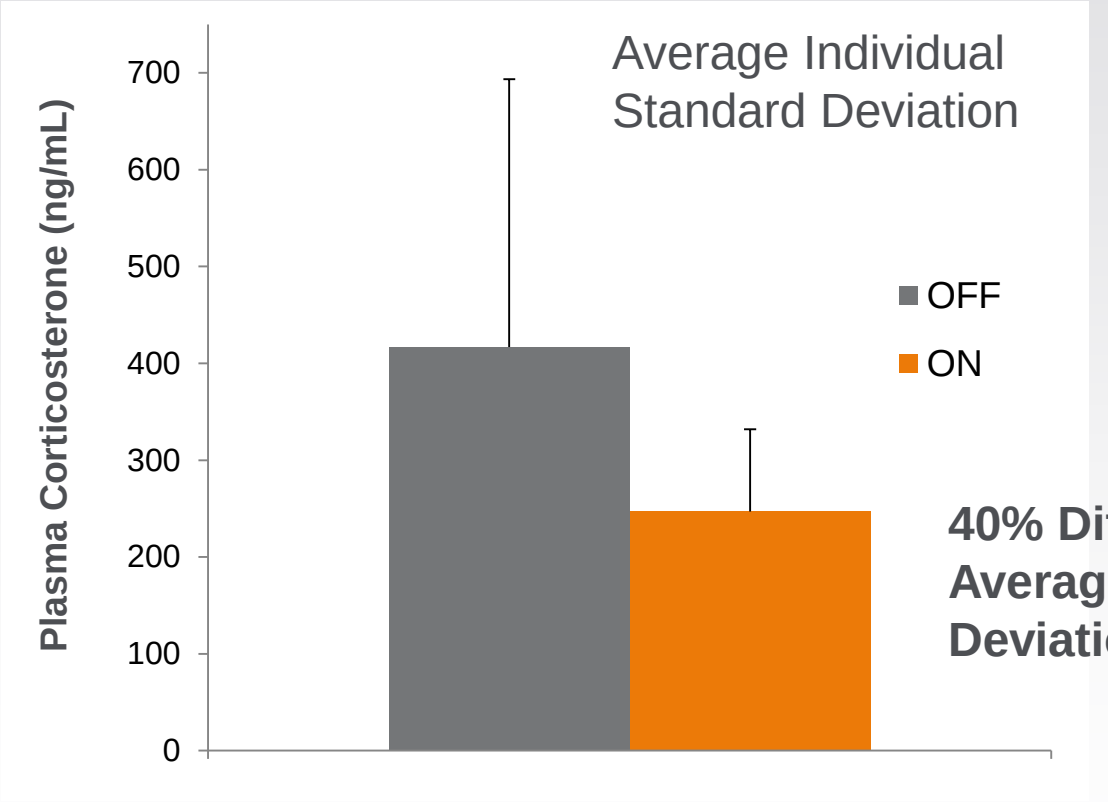
Plasma Stress Hormone Comparison

Subjects with Vibrated Needle Exhibit Lower Cort. Variability



40% Difference in Average Standard Deviation.

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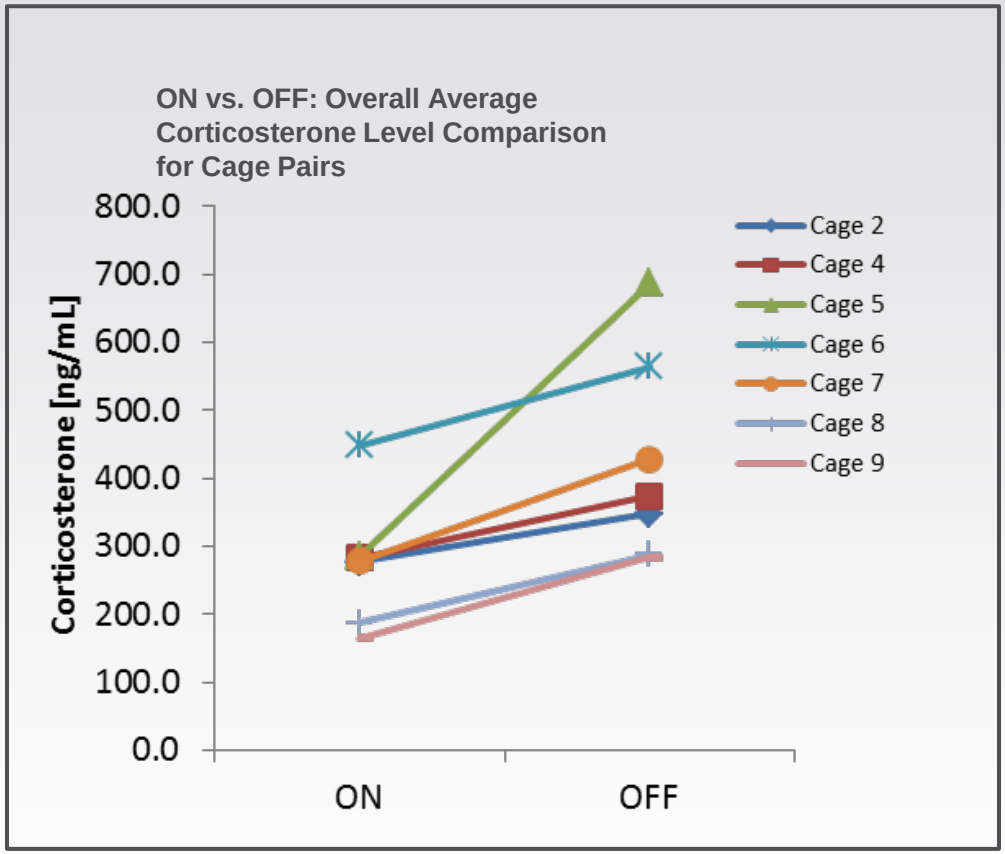
Cage Mate Comparison

Subjects with Vibrated Needle Exhibit 33.7% Lower Cort.



- Pair-housed rat comparison.
  - One sampled always with device on and the other with device off.
  - Cage 1: both subjects had device on; Cage 3: both subjects had device off, thus not shown.
- In every case, the rat sampled with device on had lower average corticosterone release.
- By a cage by cage basis, the rat sampled with device on had **33.7% lower corticosterone levels** as compared to off.

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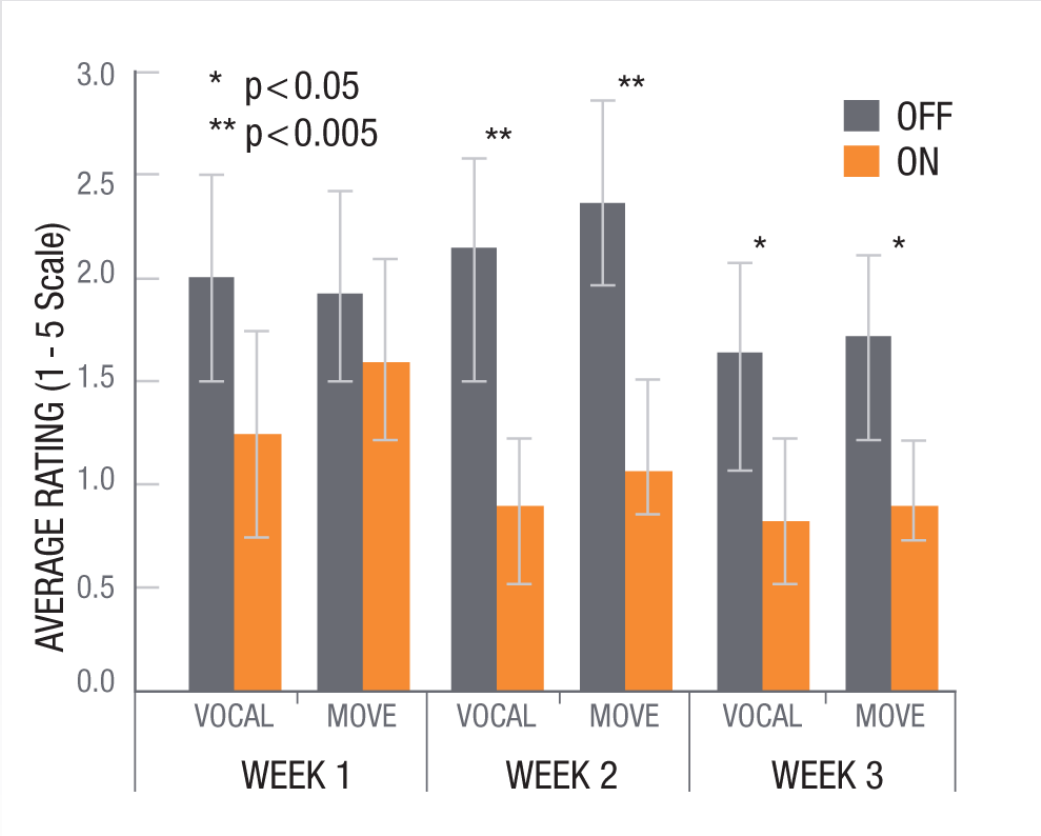
Behavioral Comparison

Subjects with Vibrated Needle Exhibit Lower Vocalization & Movement



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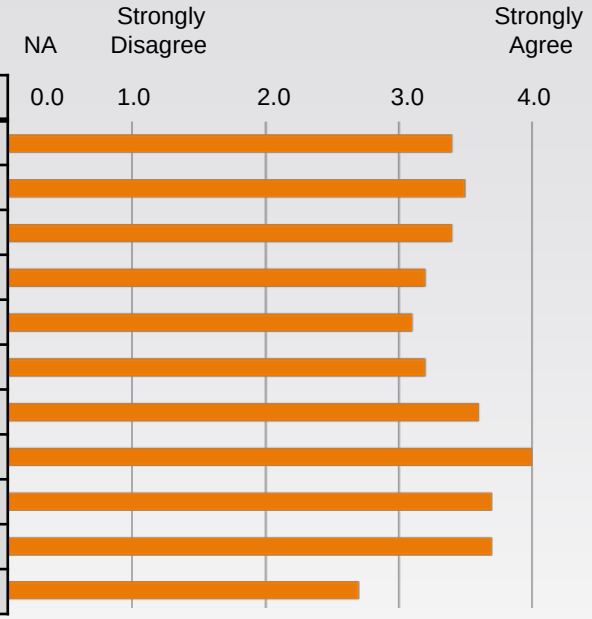
Focus Group Survey Results

End-users Agreed Reducing Subject Stress Important

	Average
In my research/practice I feel that subjects often feel discomfort during needle puncture procedures.	3.4
A device that reduces discomfort/ stress from needle puncture would be significant and valuable to me.	3.5
The device is easy to use.	3.4
The vibration of the handpiece is acceptable.	3.2
The amount of vibration of the needle is acceptable.	3.1
The size/weight of the handpiece is acceptable.	3.2
I have no concerns about being able to use the GentleSharp safely.	3.6
Needle insertion force is less with GentleSharp than with the traditional non-actuated needle/ lancet.	4.0
The device would be really useful for blood sampling.	3.7
The device could be very helpful for venous access.	3.7
The device must be cordless.	2.7



- Veterinarians, researchers, and technicians (N=9) participated in focus groups.
- The participants inserted needles into several models, including a cadaver rat tail, with and without Vibrating Needle on.
- The participants then answered a questionnaire to evaluate their experience with the Vibrating Needle, GentleSharp, and its potential.

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Study Summary

- Vibration reduced insertion force into rat tails **by up to 68%.**
- Up to **65% less stress hormone** ($p < 0.01$) observed in the blood samples obtained with the prototype turned on.
- Up to **40% less average standard deviation of individual corticosterone** measured in samples with vibration compared to without vibration.
- Statistically significant reduction in behavioral markers of stress (vocalization and movement) with vibration during venipuncture.
- Focus Group of potential end-users all agreed very strongly that the vibrated needles were easier to insert.
- Focus Group of potential end-users agreed that reducing animal discomfort and stress during blood sampling was important and that after reviewing the data and trying device believed it has value.
- Supports **R**eduction and **R**efinement of animal studies that require blood sampling.

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Current/Future Work

- Ongoing study at Penn State University with mice to evaluate other sampling sites.
- Ongoing study at Medical University of South Carolina to evaluate tail blood sampling of mice.
- 12-month longitudinal serial blood sampling study at the Pennsylvania State University, starting December 2013.
- The Vibrating Needle Device, GentleSharp anticipated product launch January 2014.

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Thank You to:

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+ National Institutes of Health, National Institute on Aging SBIR Program.
+ And to you for your time today!

Questions??

GentleSharp™

GentleSharp can be previewed at **Booth 2143** in the Exhibit Hall.

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