



Venous Congestion Countermeasure Study (VCCM)

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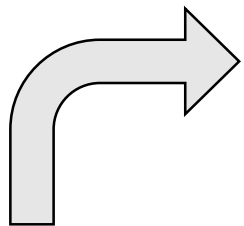
Human Research Program Investigators' Workshop

Galveston, TX

January 27-30, 2020

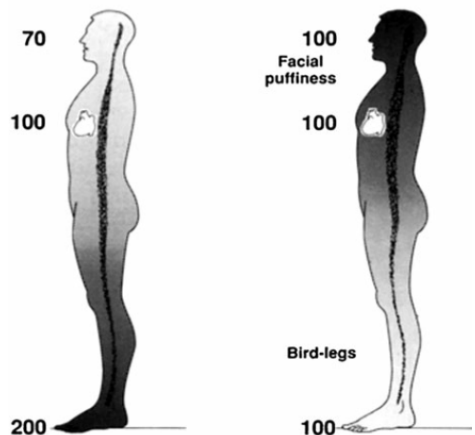


Headward Fluid Shift Hypothesis

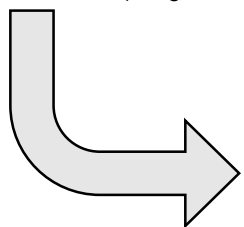


Elevated ICP

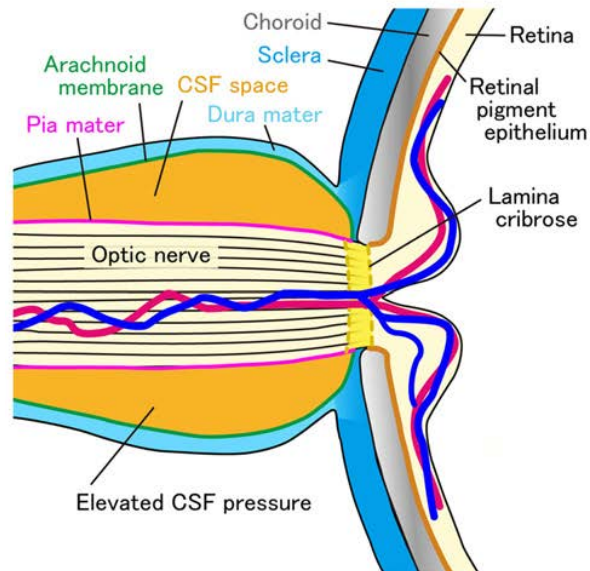
Earth Weightlessness



(Hargens, *Eur J Appl Physiol*, 2013)



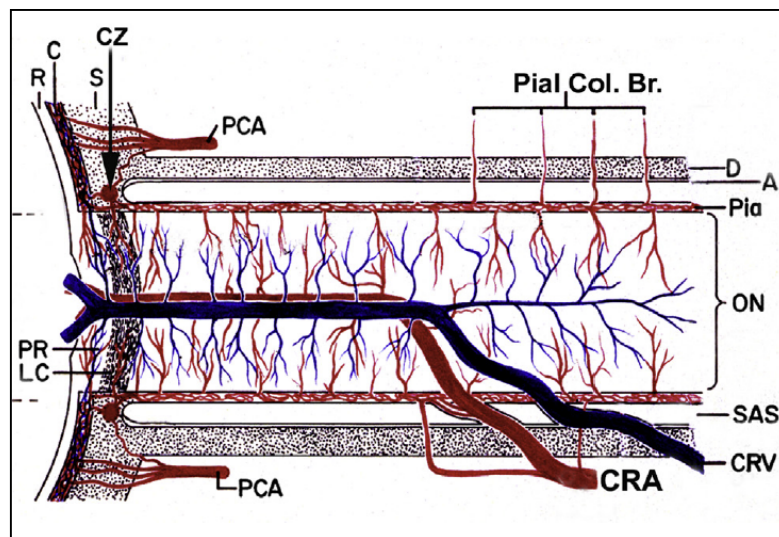
Vascular Effect



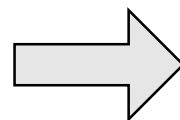
(Nakashima et al., 2013)



Axoplasmic stasis
Neuronal swelling



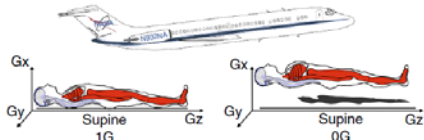
(Hayreh, 2016)



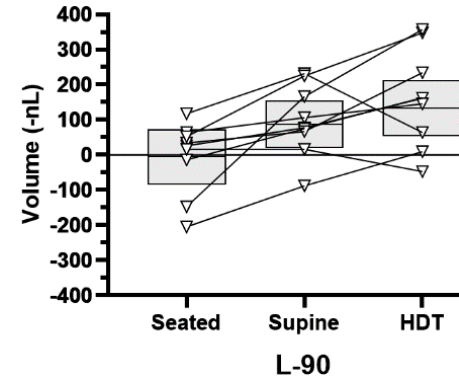
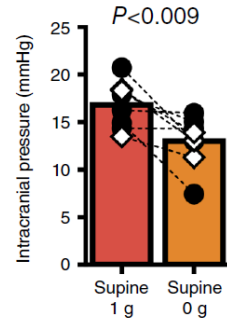
Increased capillary filtration
Accumulation of extravascular fluid



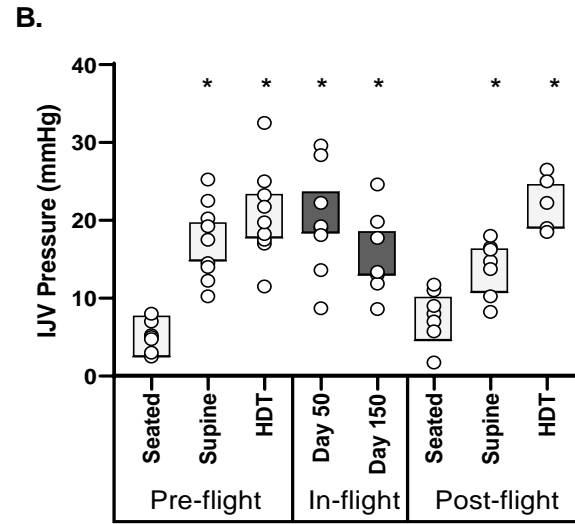
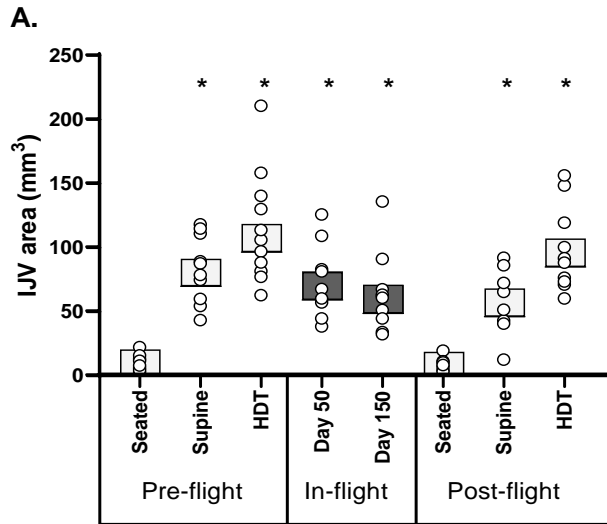
Intracranial Pressure During Weightlessness



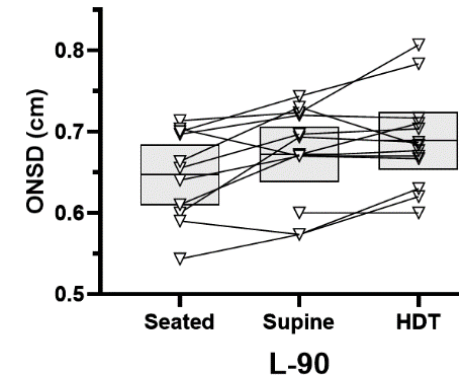
(Lawley et al., 2017)



L-90



(Marshall-Goebel et al., 2019)



(Preliminary Data, Fluid Shifts Study)

ICP appears similar to, or less than, Supine posture on Earth; not pathologically elevated. Sustained over 24 hours without daily posture-induced lowering of ICP.

Countermeasures

- NASA & the SANS community are currently searching for the best countermeasure to reverse the headward fluid shift during spaceflight.
- Promising spaceflight-compatible techniques:
 - Lower Body Negative Pressure (LBNP)
 - Veno-constrictive thigh cuffs (VTC)
 - Impedance threshold device (ITD; resistance breathing mask)
- Novel combined countermeasure approach



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VCCM Specific Aims

1. Determine if **individual countermeasures** are able to acutely reverse a seated-to-supine posture induced headward fluid shift
2. Determine if the use of **combined countermeasures** can acutely reverse a seated-to-supine posture induced headward fluid shift.



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VCCM Study Overview



3-Part Study:

1. **CVL** (PI: Stenger): Study of individual and combined countermeasures
2. **UTSW** (PI: Levine): 3 day -6 degree HDT bedrest study with -20 mmHg LBNP (sleep sack) during sleep for 8 h

Lower body negative pressure during sleep safely attenuates choroid engorgement associated with simulated microgravity - 20520	Jan 28th, 2020	3:24 PM - 3:42 PM	Grand Ballroom B	SANS Research and Medical Updates
Can nightly prolonged lower body negative pressure preserve plasma volume during simulated microgravity? - 20361	Jan 27th, 2020	4:30 PM - 6:00 PM	Exhibit Hall A	Poster Session A: Spaceflight Associated Neuro-ocular Syndrome

3. **UCSD/UTHSD-Houston** (PIs: Hargens/Kramer): MRI study of most effective combined countermeasure (TBD from **CVL** study)

Venous congestion countermeasure study	Jan 27th, 2020	4:30 PM - 6:00 PM	Exhibit Hall A	Poster Session A: Spaceflight Associated Neuro-ocular Syndrome
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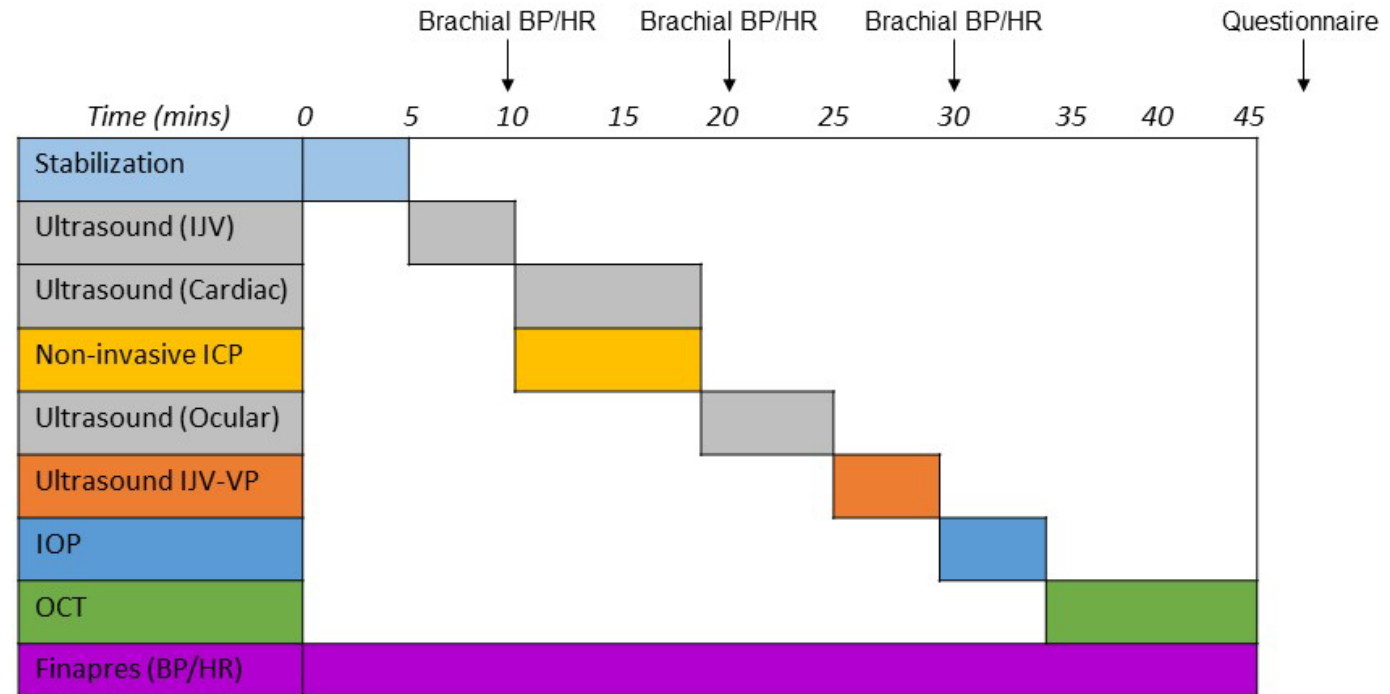


VCCM Study Overview

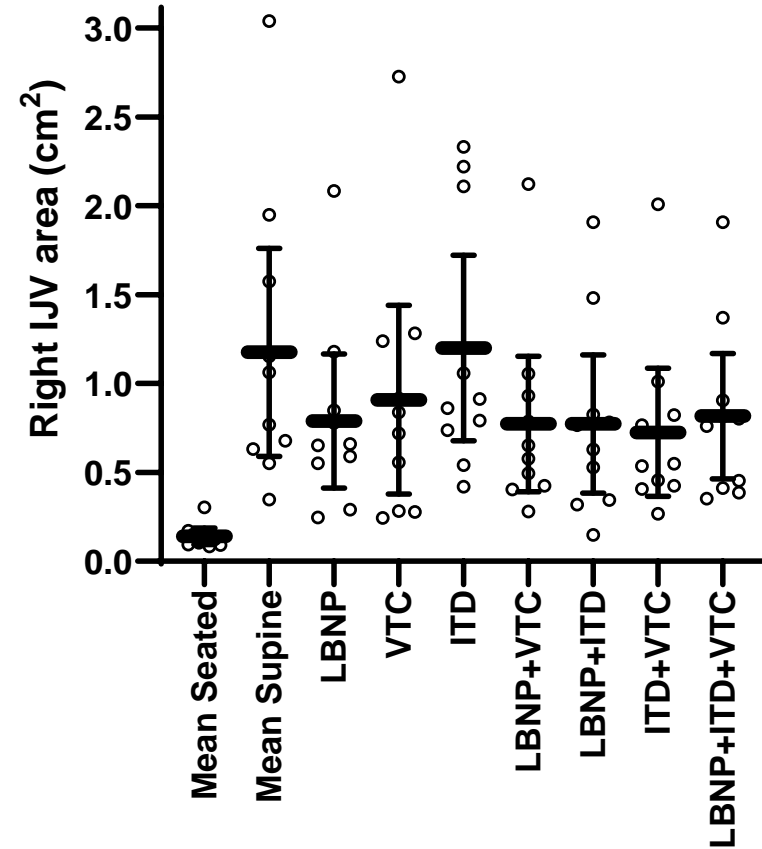
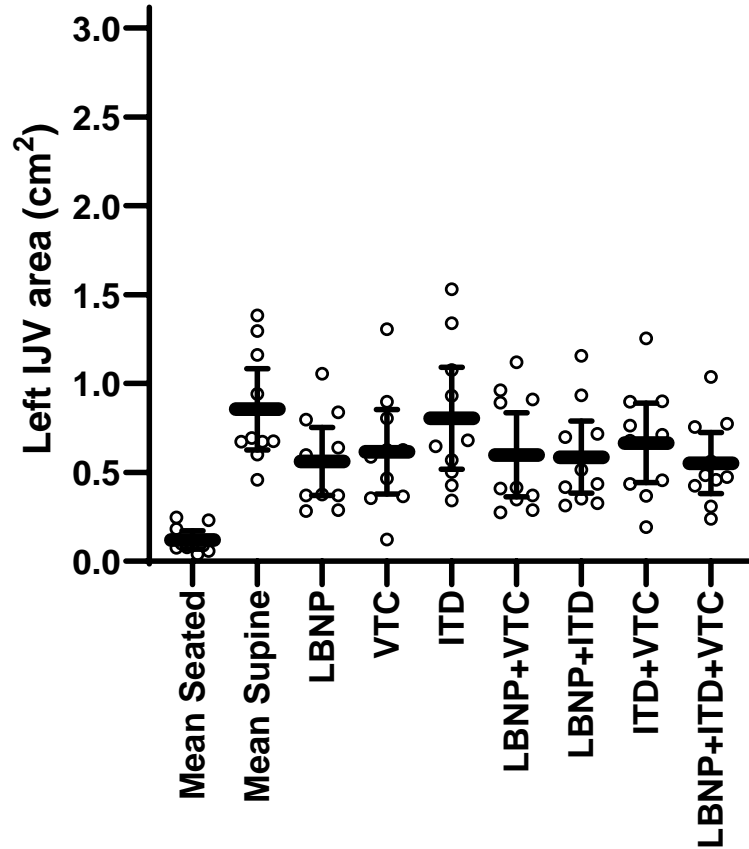
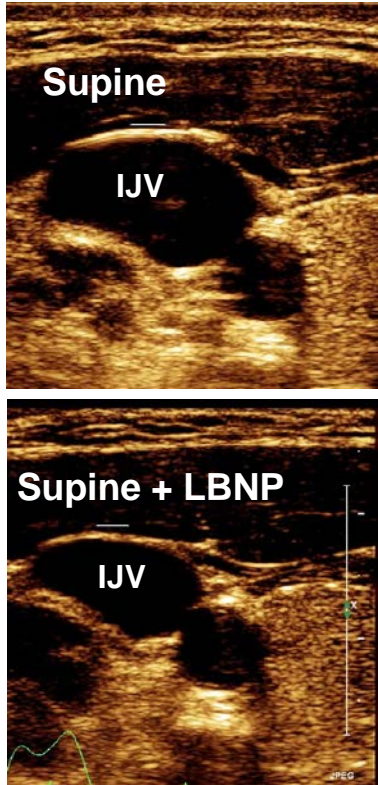
CVL Study:

- N = 10 subjects (M/F), ages 30-55
- Cross-over design study with 7 interventions over 3 test days

Day 1 (randomized order)	{	1. <i>LBNP</i>
		2. <i>VTC</i>
		3. <i>ITD</i>
Days 2 & 3 (randomized order)	{	4. <i>LBNP + VTC</i>
		5. <i>LBNP + ITD</i>
		6. <i>ITD + VTC</i>
		7. <i>LBNP + VTC + ITD</i>



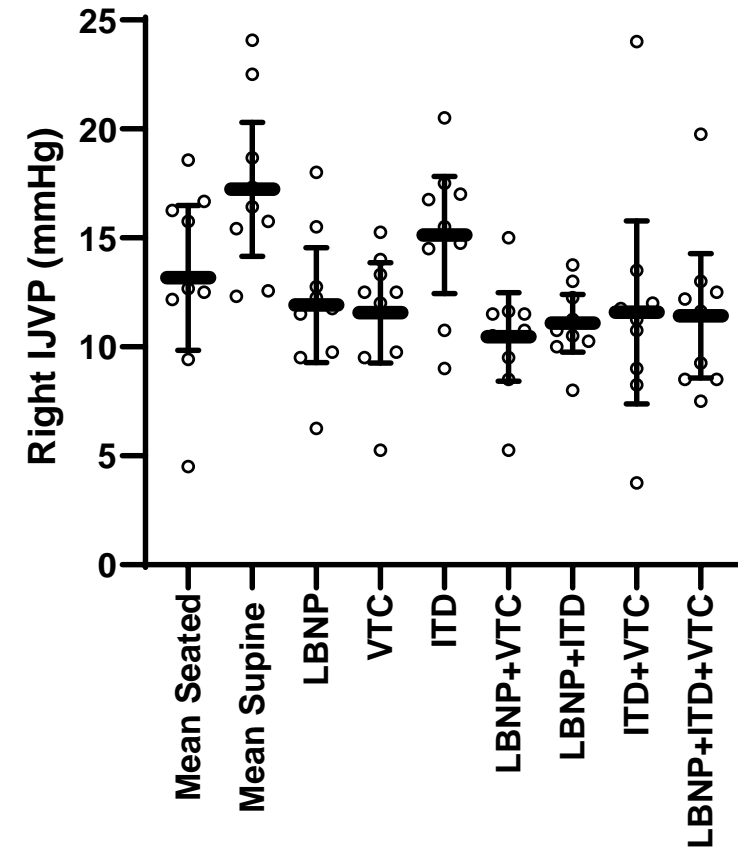
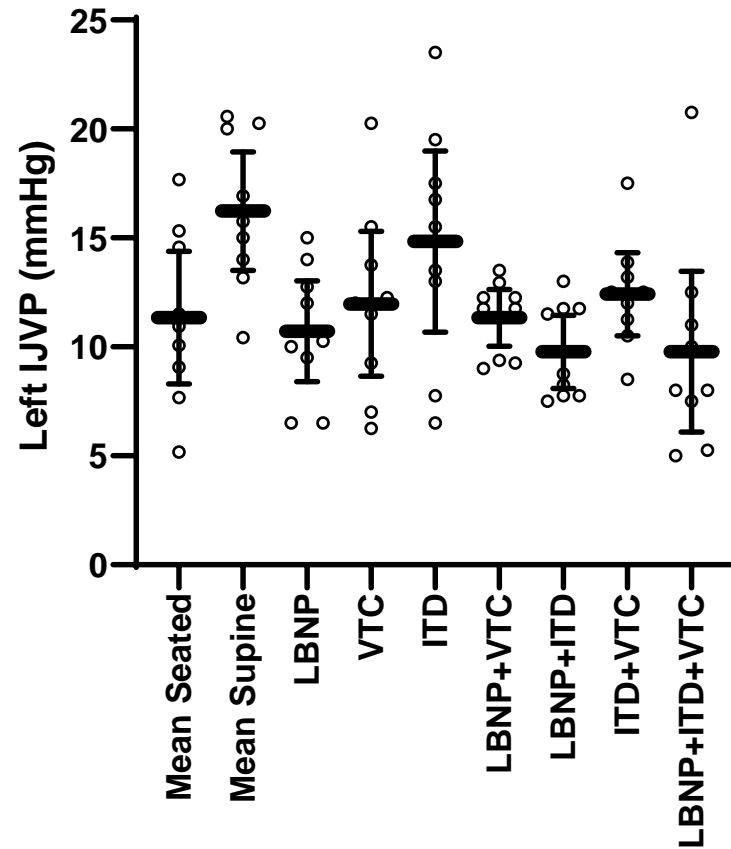
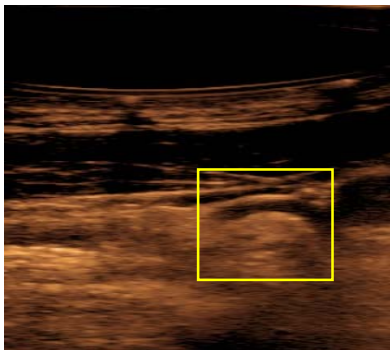
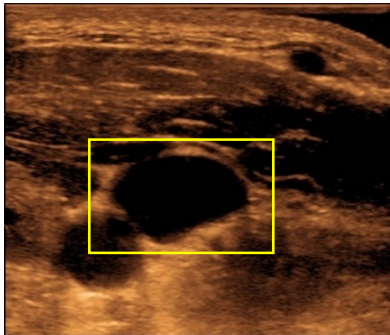
IJV Area at End-Expiration



- LBNP & VTC decrease IJV area by a similar magnitude
- ITD does not decrease IJV area
- Combined countermeasures do not provide additive effect over single countermeasure

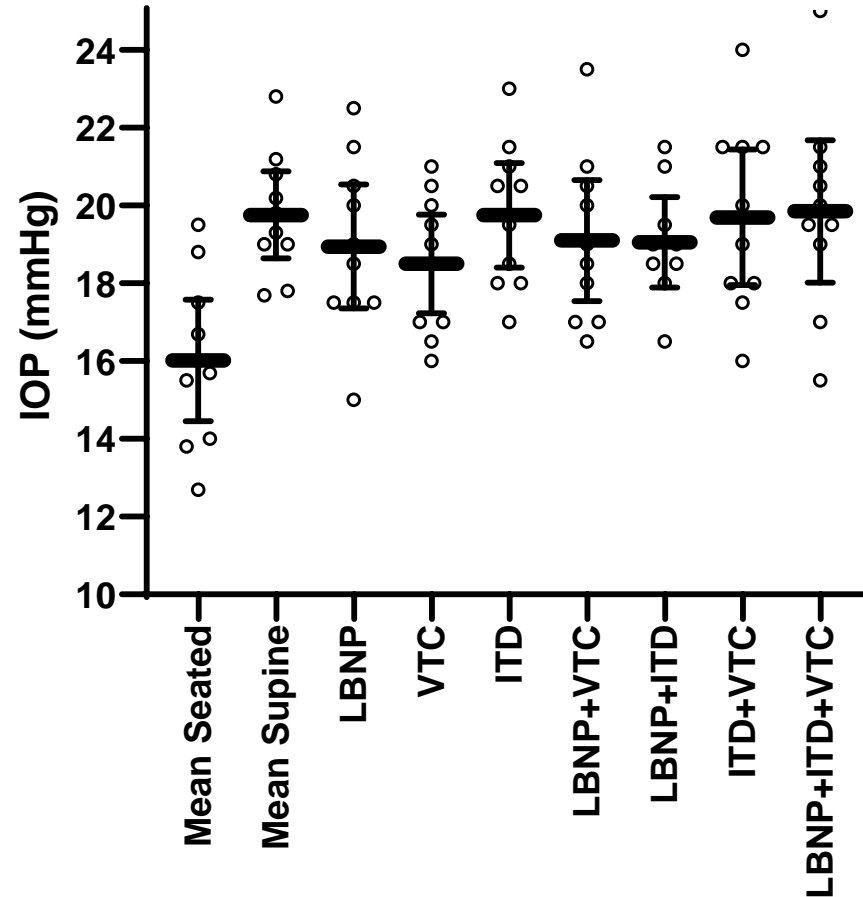
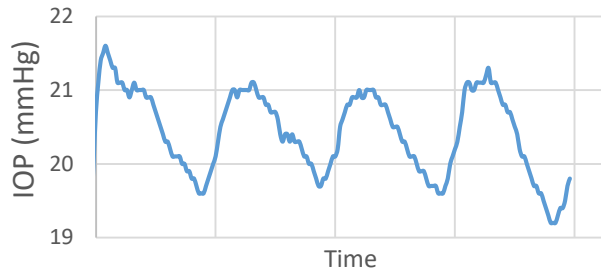
(bars are mean \pm 95% CI)

Non-invasive IJV Pressure



- LBNP & VTC decrease IJV pressure by a similar magnitude (bars are mean \pm 95% CI)
- ITD does not decrease IJV pressure
- Combined countermeasures do not provide additive effect over single countermeasure

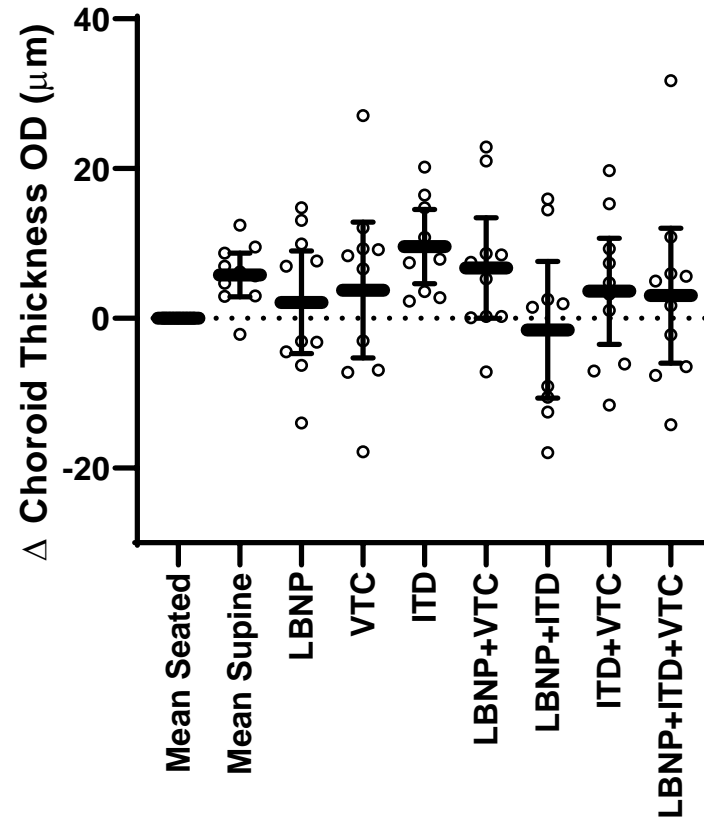
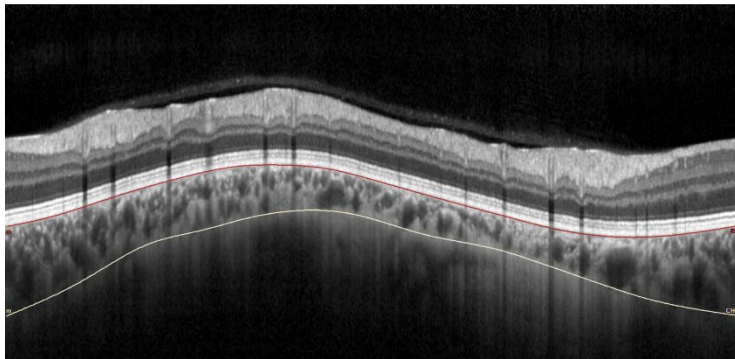
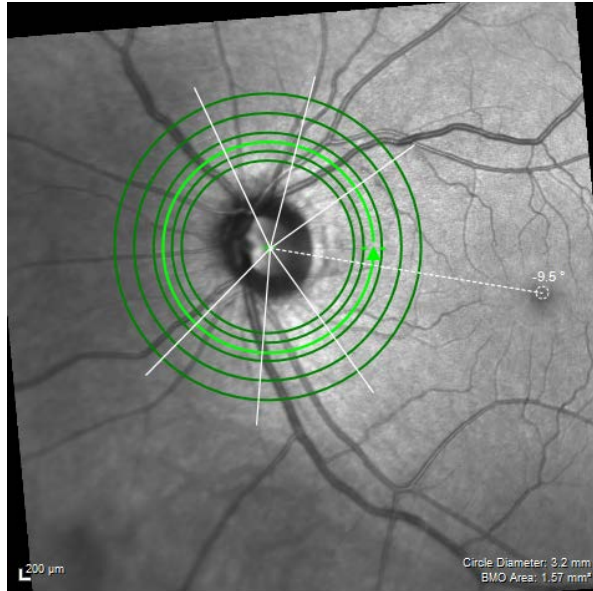
Intraocular Pressure



(bars are mean \pm 95% CI)

- LBNP & VTC decrease IOP by a similar magnitude
- ITD does not decrease IOP
- Combined countermeasures do not provide additive effect over single countermeasure

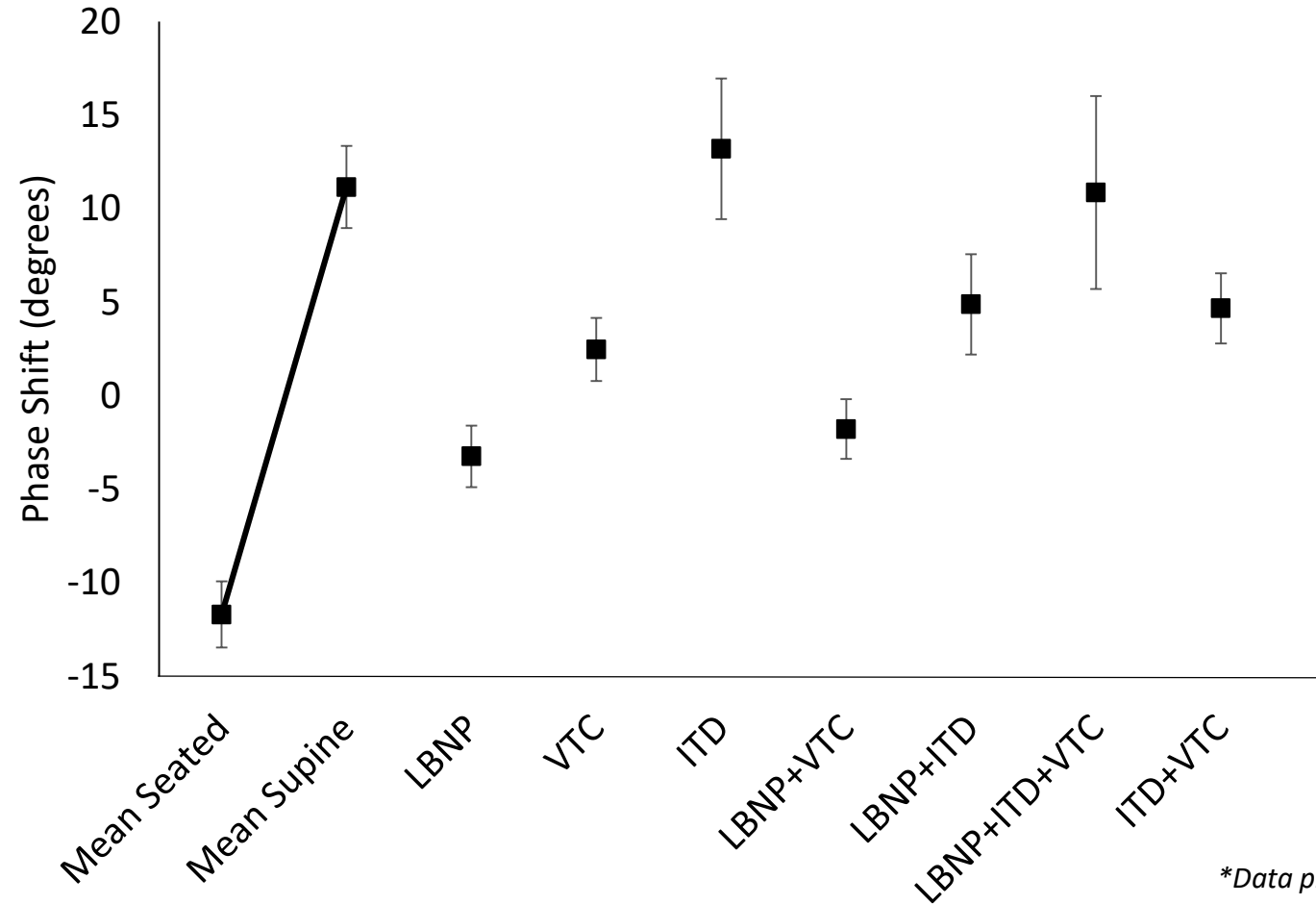
Choroid Thickness



(bars are mean ± 95% CI)

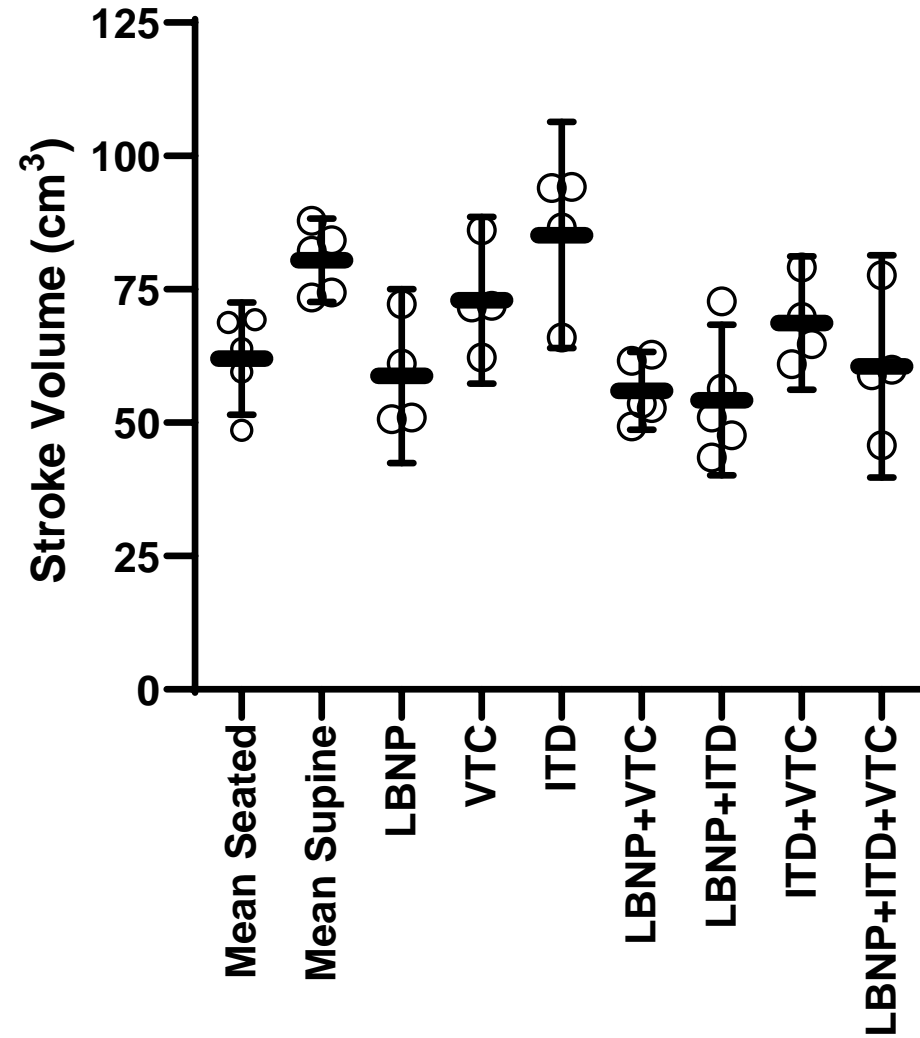


OAE



**Data presented as mean ± SE*

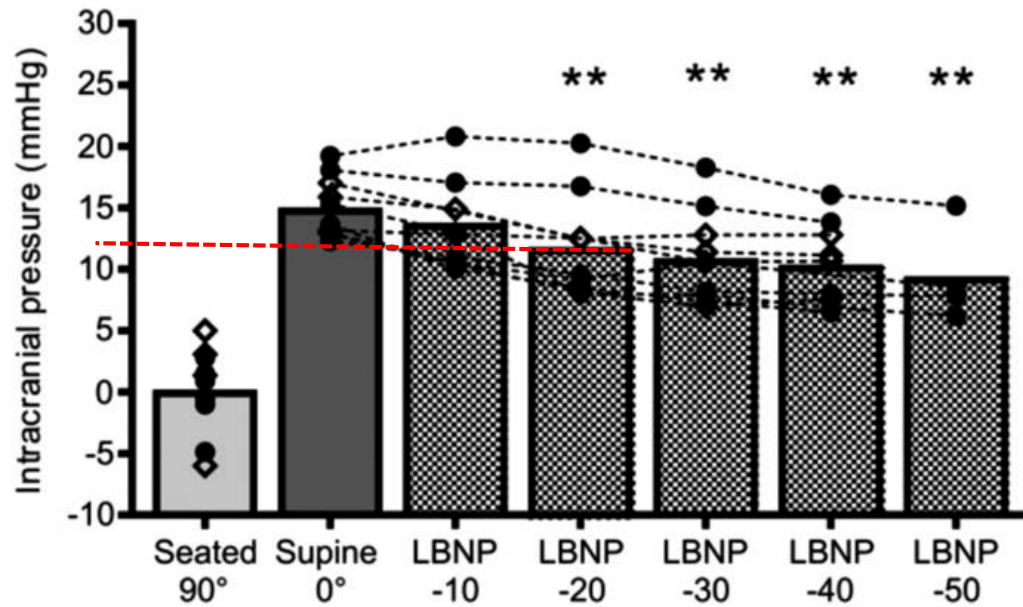
Stroke Volume



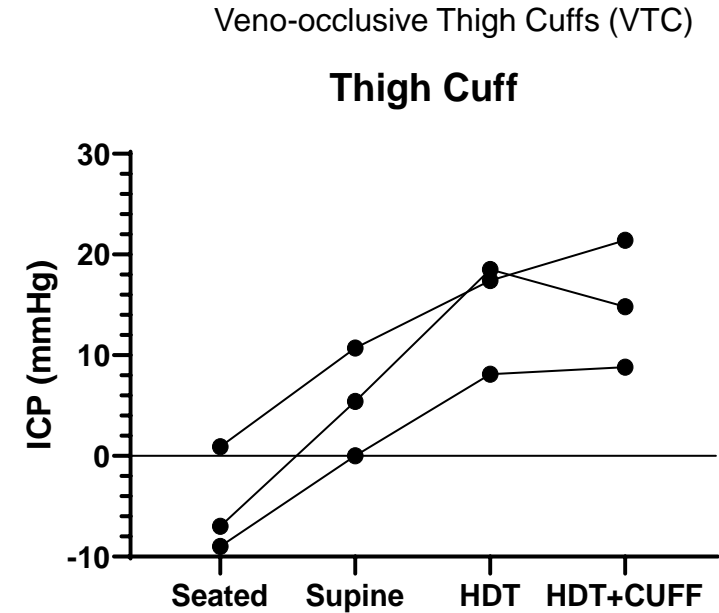
(bars are mean ± 95% CI)

*n=5

Changes in ICP with Countermeasures

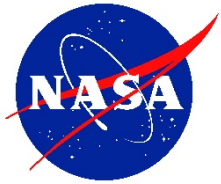


(Petersen, et al. *J Physiol*, 2019)



(Unpublished data courtesy of Brandon Macias)

- LBNP lowers ICP in the supine posture
- Veno-occlusive thigh cuffs do not decrease ICP in HDT position



Discussion

- LBNP and VTC appear to be the most effective countermeasures to attenuate the venous fluid shift associated with supine posture
- Combined countermeasure approach does not significantly enhance countermeasure effect compared to LBNP alone.
- Duration of headward fluid shift countermeasure needed is unknown
- Future work:
 - UT/UCSD VCCM MRI study (PI: Hargens; ~Feb 2020)
 - UTSW VCCM LBNP during sleep study (PI: Levine; ongoing)
 - 30-day :envihab strict HDT bedrest SANS countermeasure study



Acknowledgements



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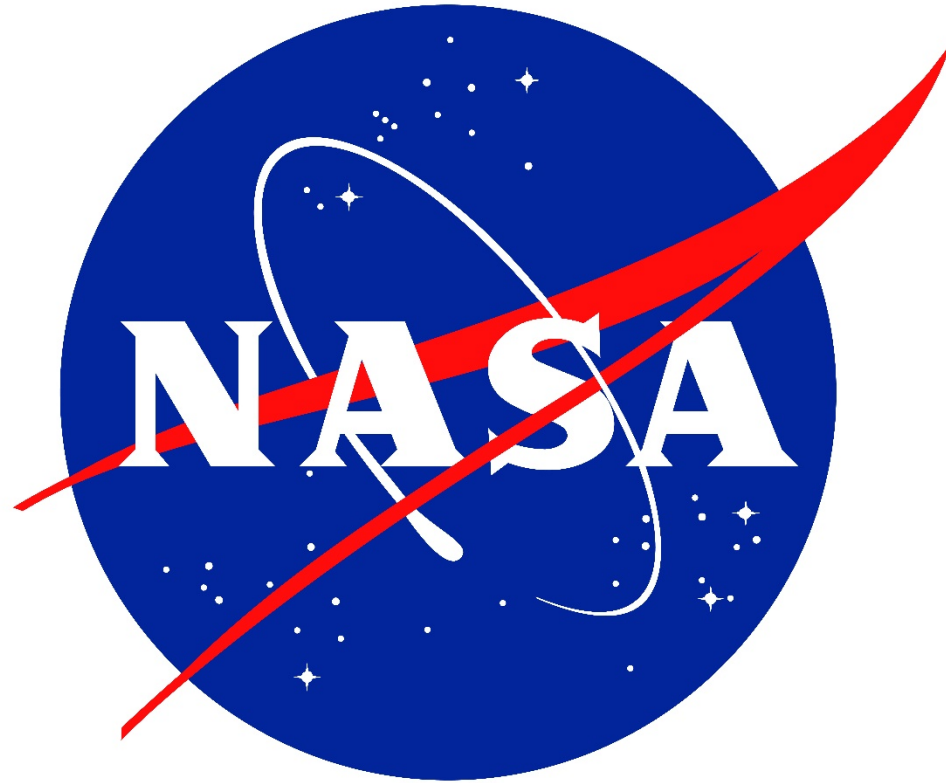
Nimesh Patel

Baylor College of Medicine

Richard Danielson



NASA JSC
Cardiovascular & Vision Laboratory



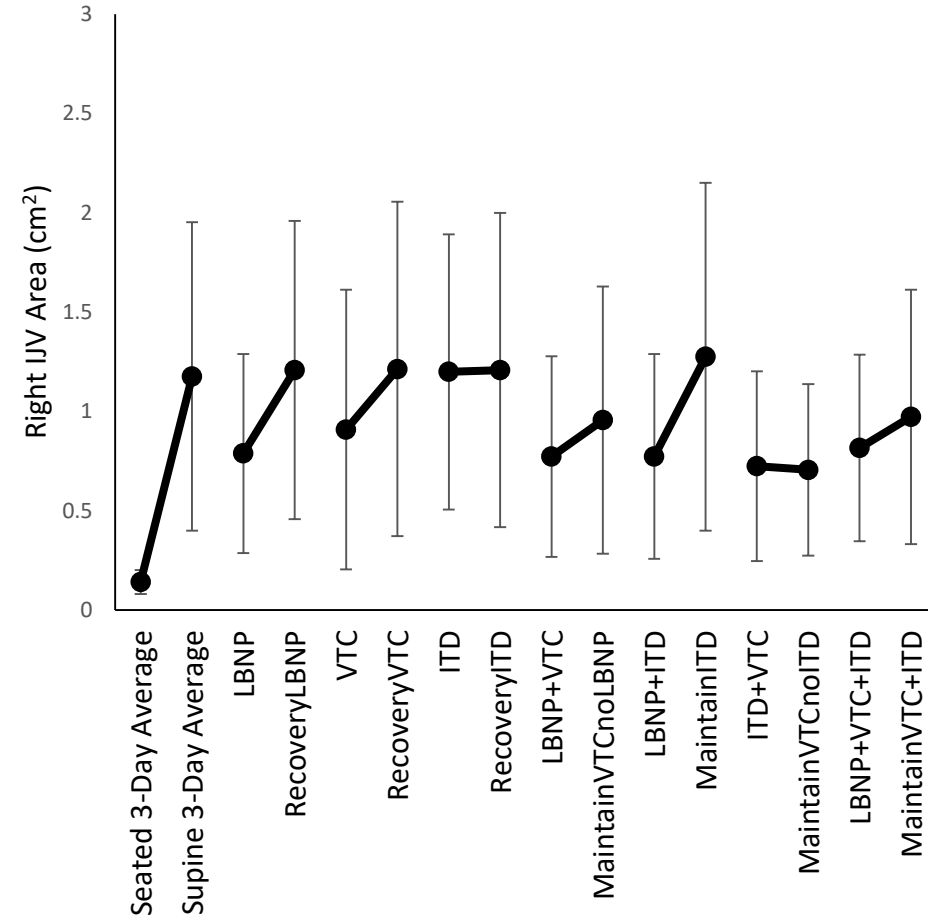
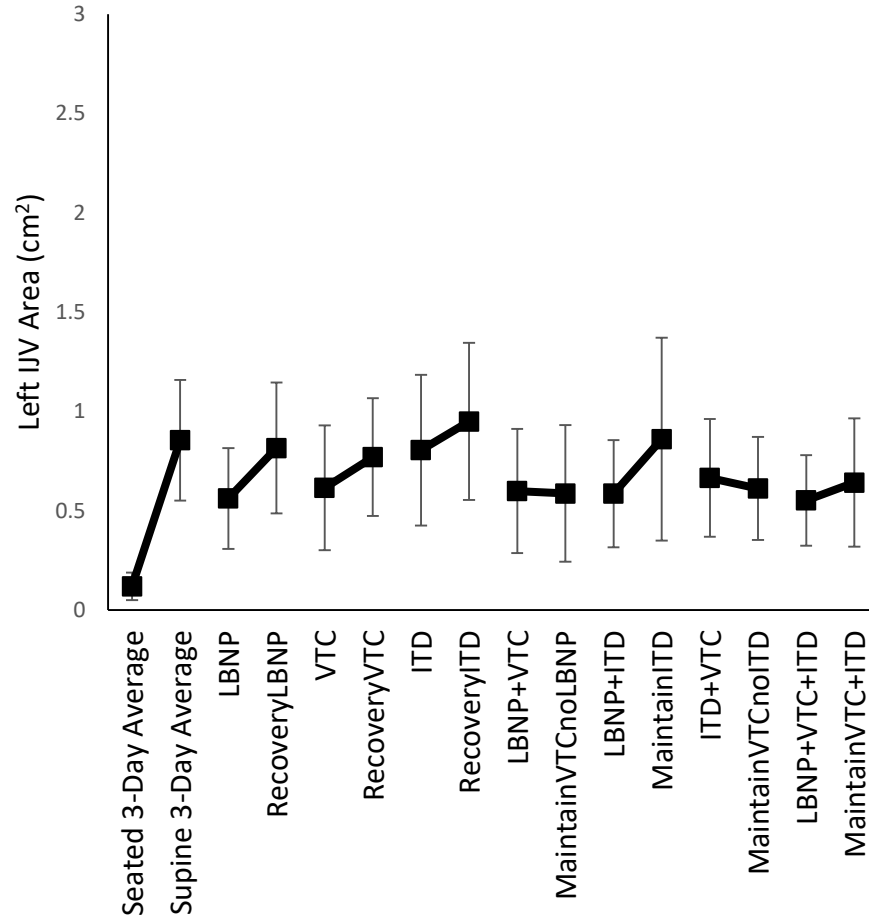


Backup Slides



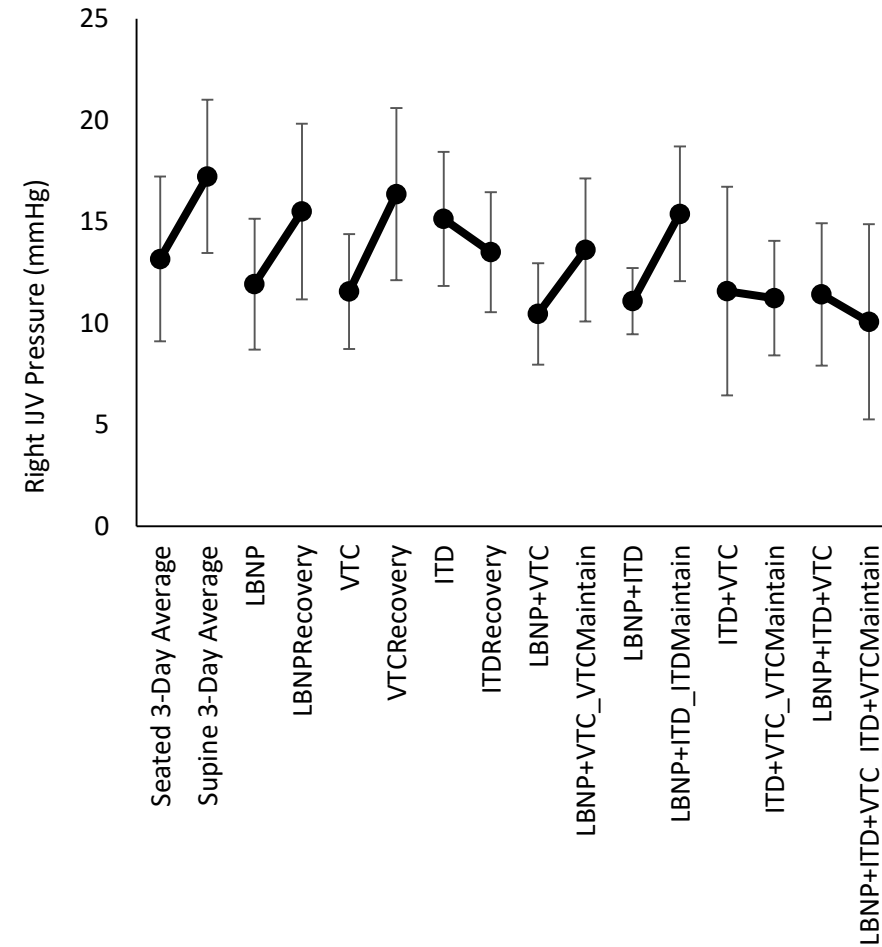
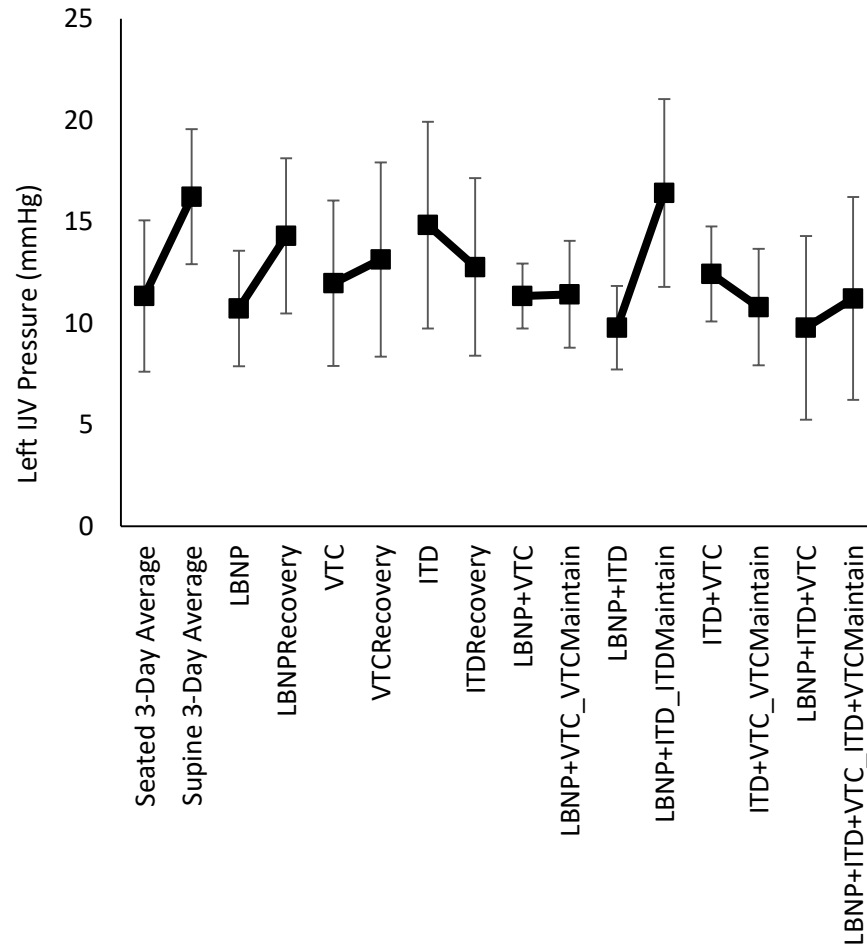


IJV Area with Maintained Countermeasures

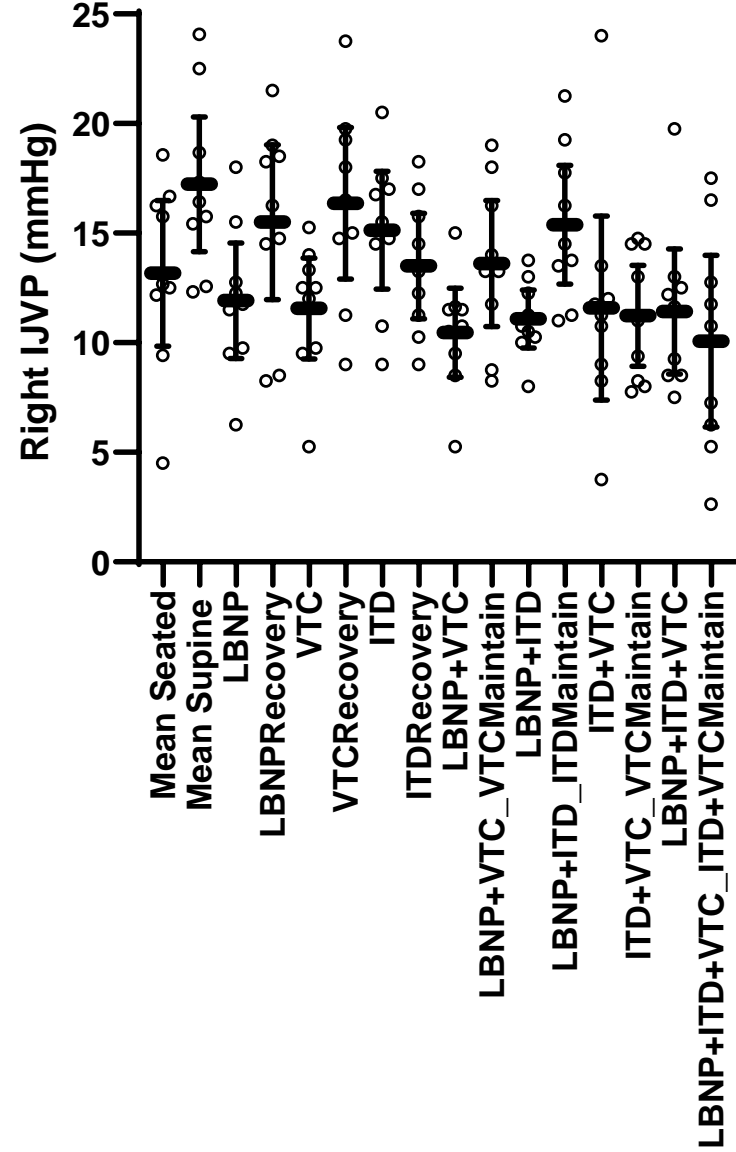
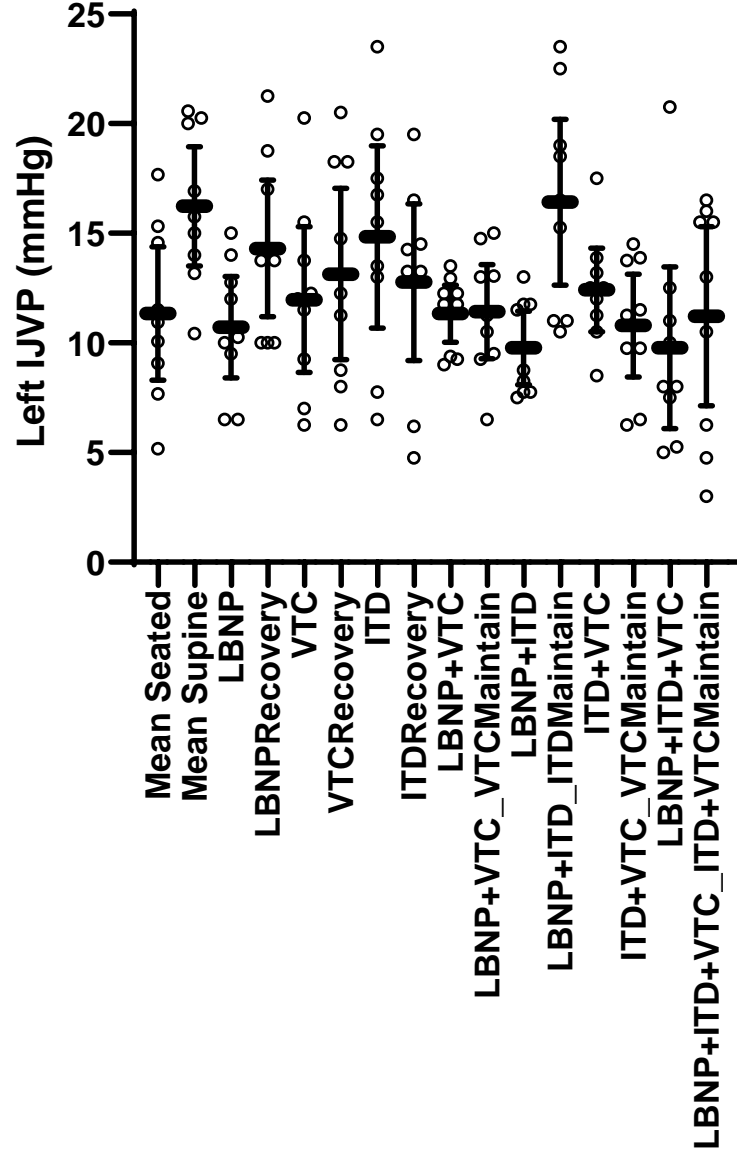




IJV Pressure with Maintained Countermeasures

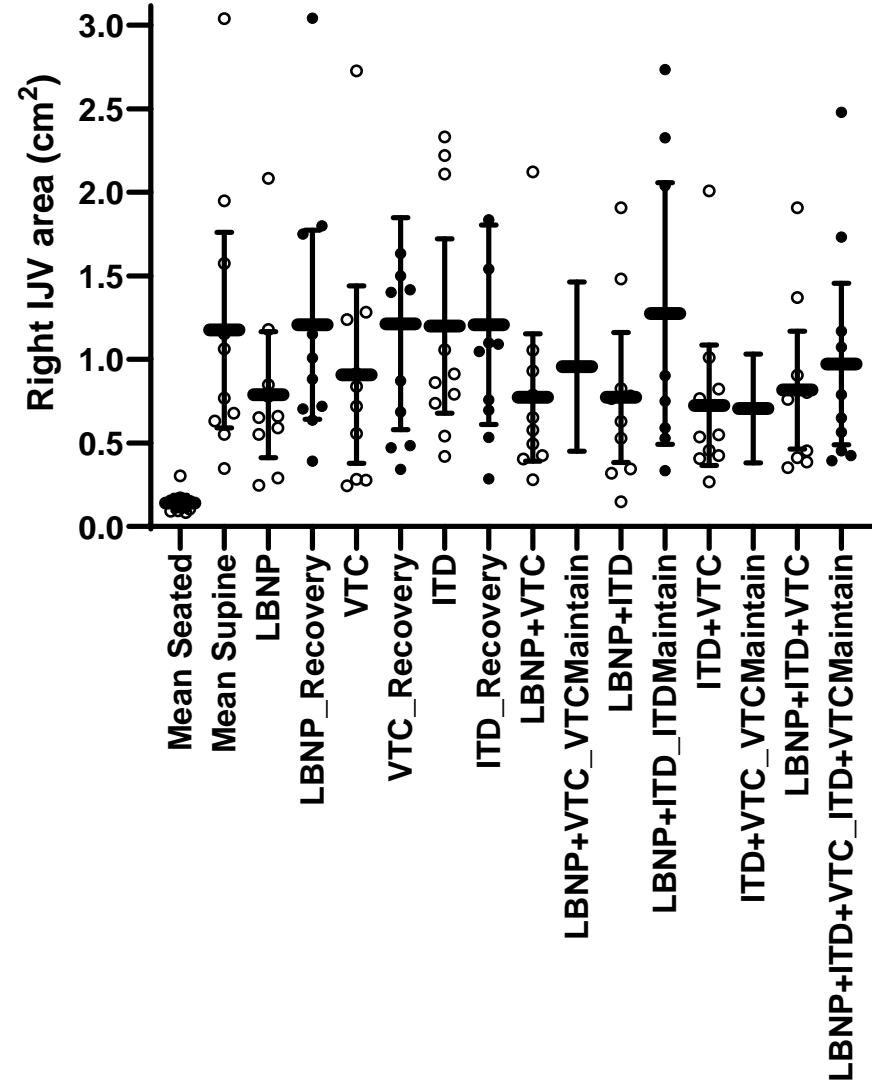
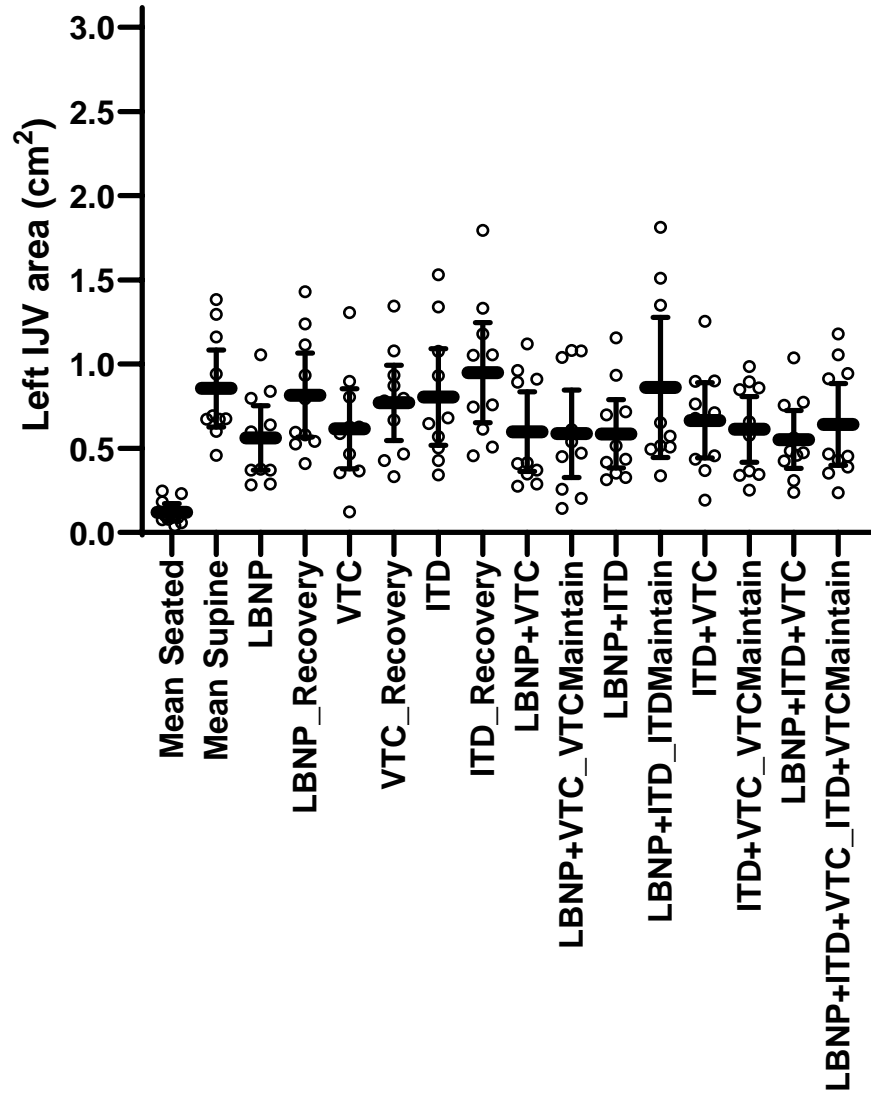


IJV Pressure with Maintained Countermeasures





IJV Area with Maintained Countermeasures



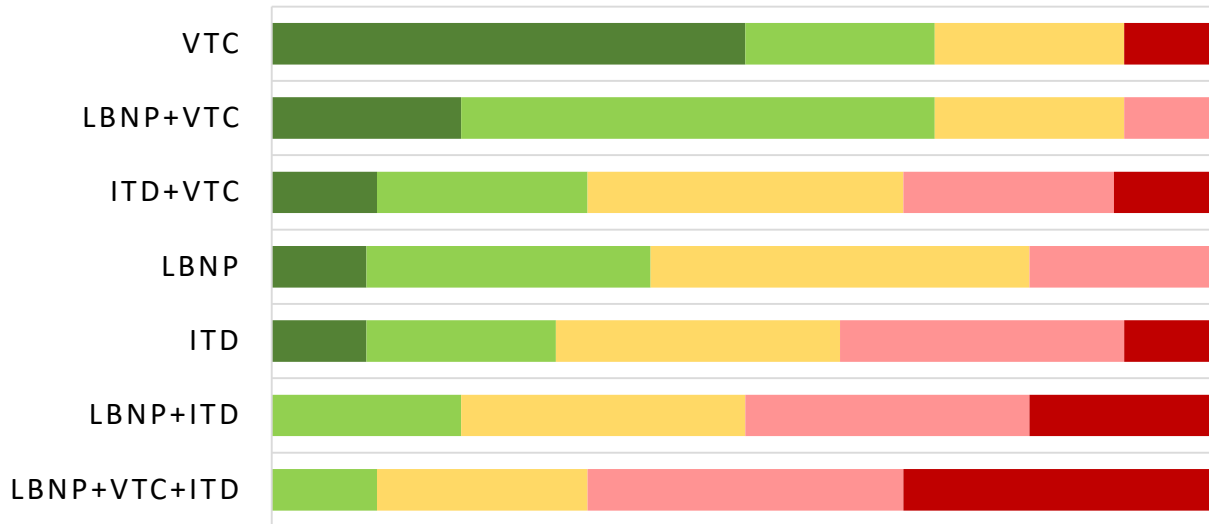


Results: Subject Questionnaire



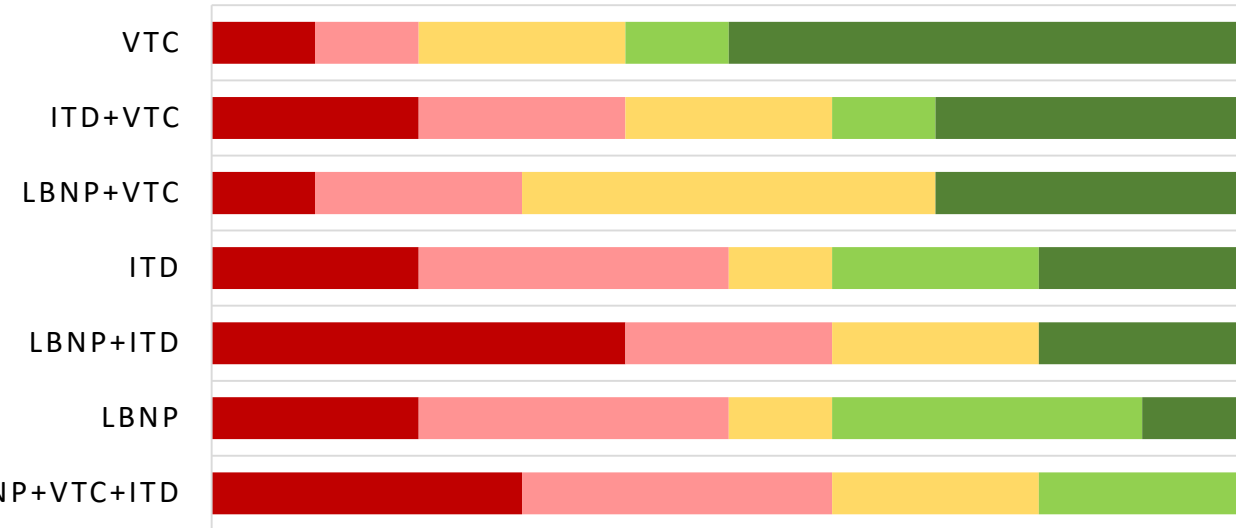
COUNTERMEASURE COMFORT

VERY COMFORTABLE 1 2 3 4 5 VERY UNCOMFORTABLE



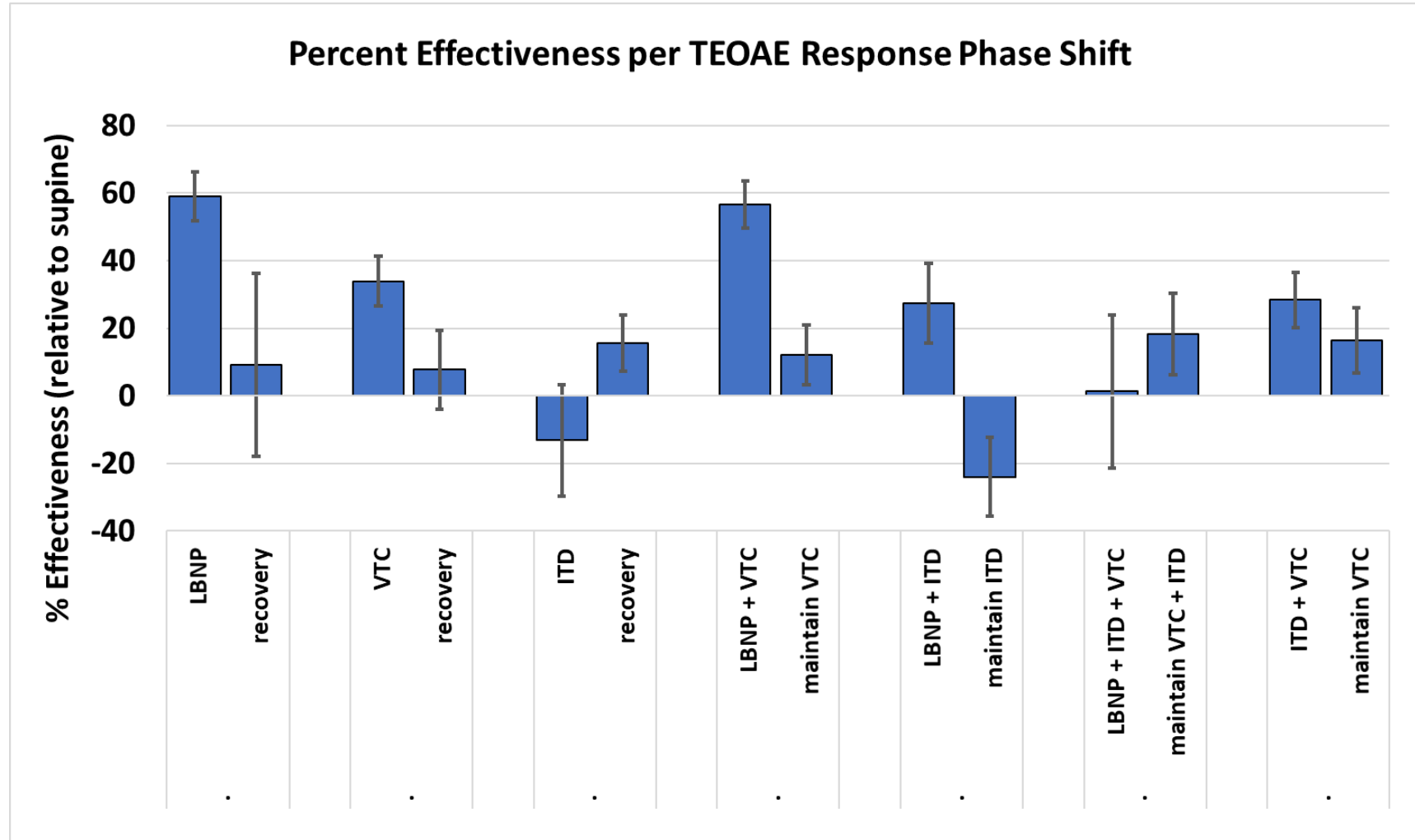
DURATION OF COMFORTABLE WEAR

< 30 min 30 min - 59 min 1 hr - 1 hr 59 min 2 hr - 2 hr 59 hrs 3+ hrs

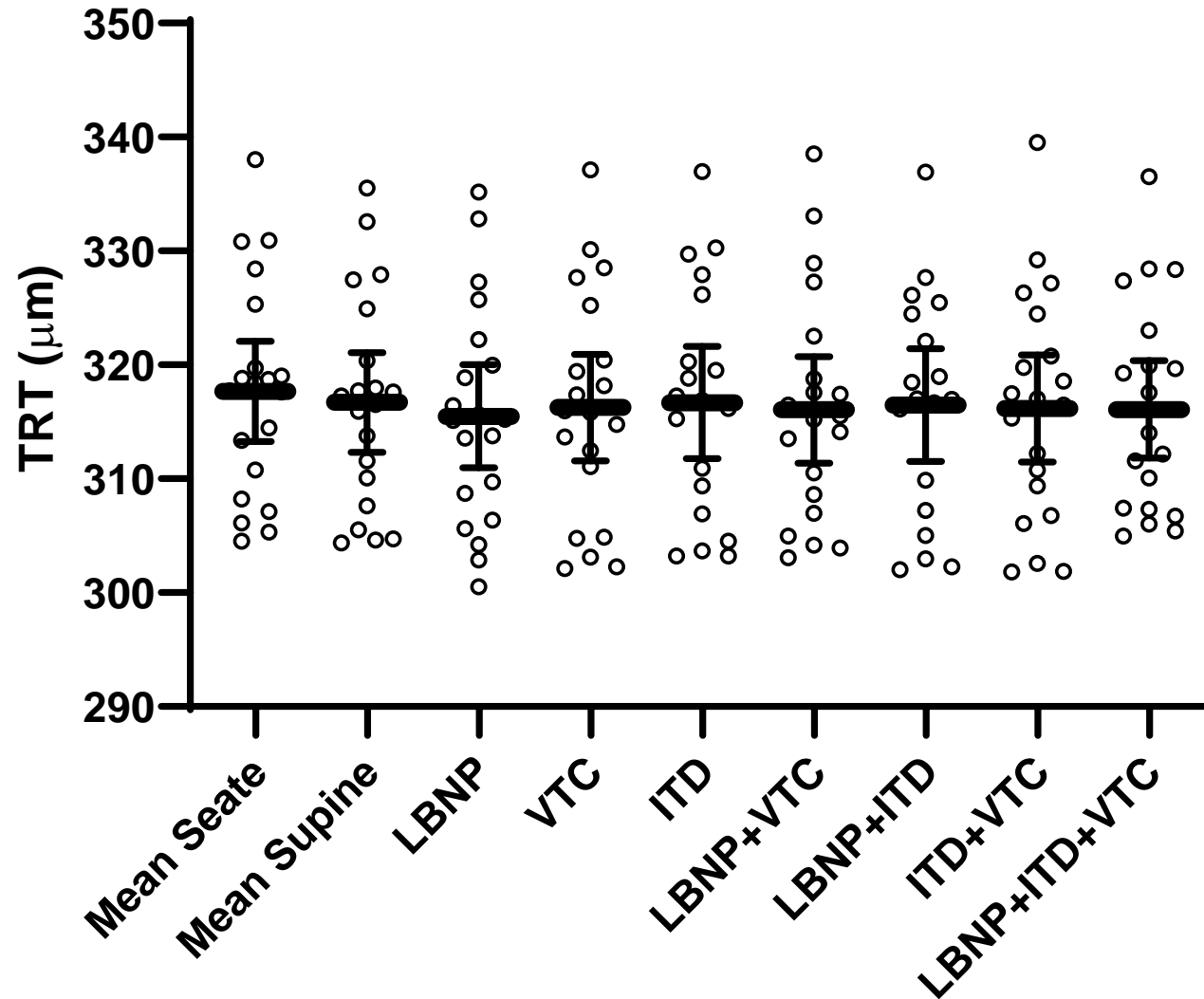


- Individual anatomical differences likely accounts for differences in comfort perception of countermeasures (VTC and LBNP)

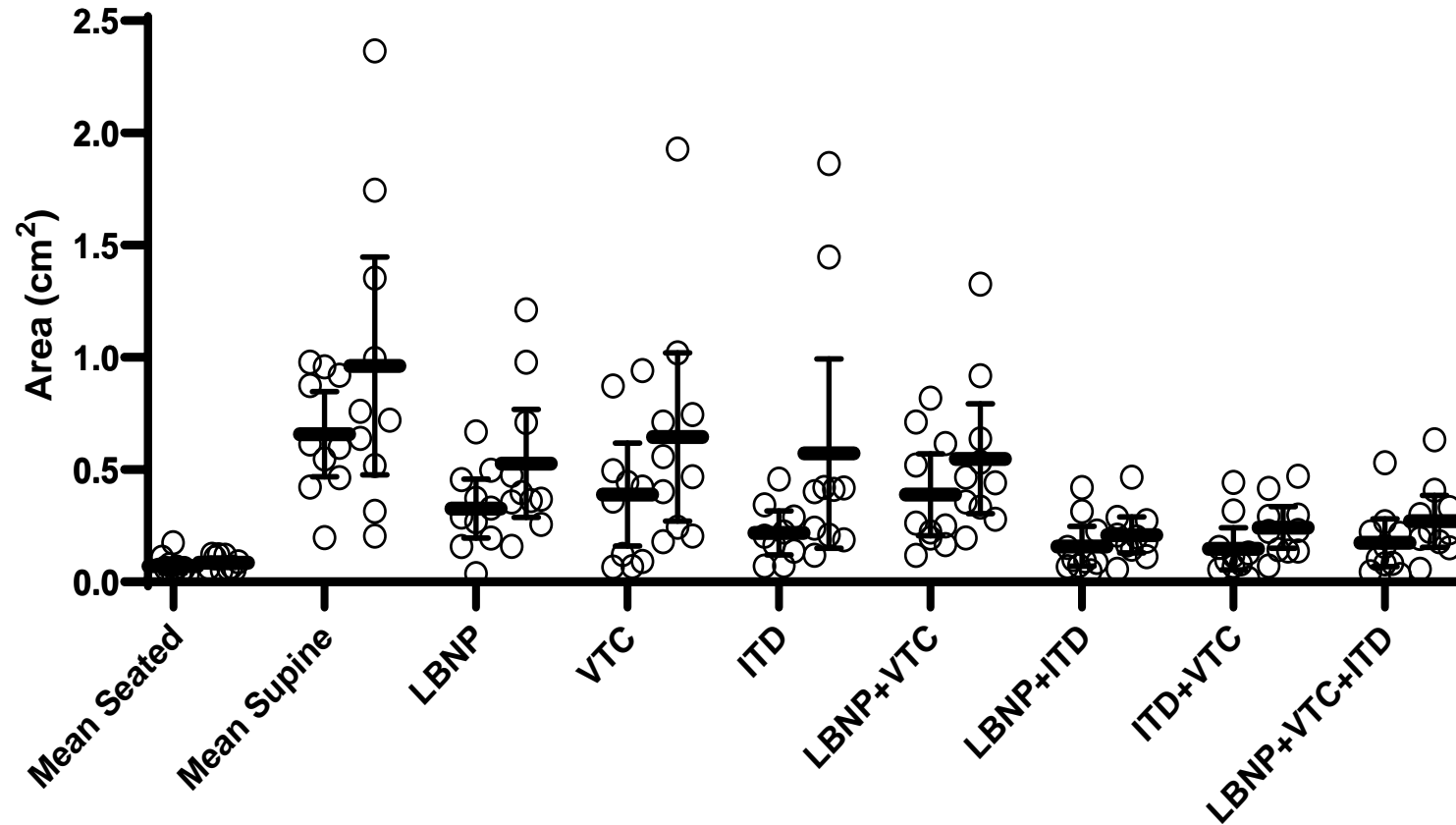
Results: OAE



Total Retinal Thickness



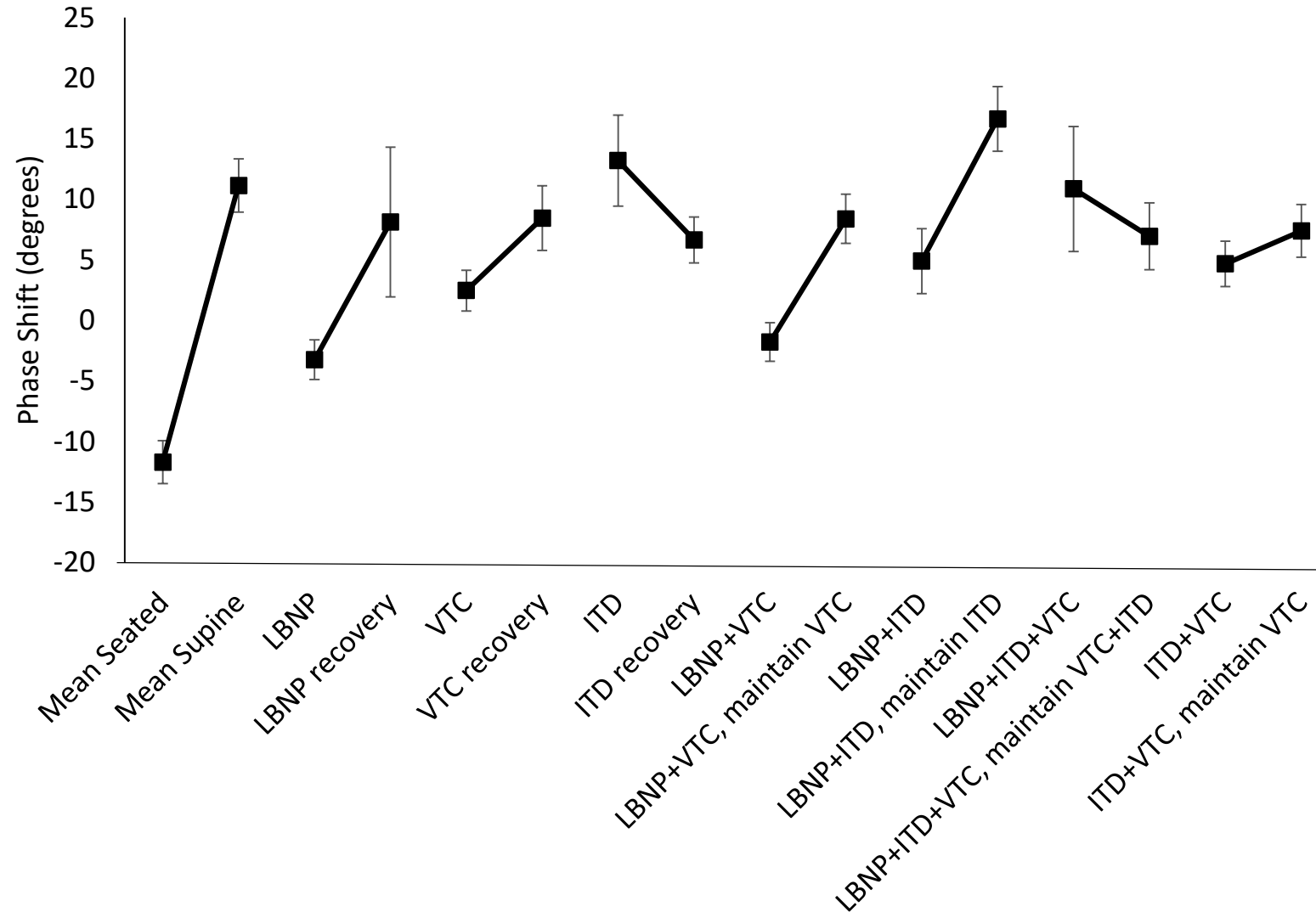
Results: IJV Area (End Inspiration)



Bilateral measurement (graph shows left and right IJV)



Results: OAE





Schedule for 1 Subject

