

Identifying risk factors for silicone oil droplets in anti-VEGF injections: a quantitative in vitro study

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Summary

- ▶ Intravitreal injections:
 - ▶ Silicone oil (SiO) droplets are released by syringes
- ▶ Purpose:
 - ▶ To examine potential risk factors of release of silicone oil droplets in anti- VEGF injections
- ▶ Methods:
 - ▶ Quantitative in-vitro study
 - ▶ Study the source of silicone oil droplets: compounding, delivery syringe
 - ▶ Impact on the quantity of SiO: technique, drug

Summary

▶ Conclusions:

- ▶ Compounding processes can be a source of SiO droplets
- ▶ Variability between the 3 anti-VEGF agents
- ▶ Variability between insulin syringes

Introduction

- ▶ Silicone oil (SiO) droplets are released by syringes and found in the vitreous of patients that received intra-vitreal injections (Bakri and Ekdawi, 2008; Freund et al., 2006).
- ▶ These droplets can lead to:
 - ▶ Complaint of floaters that, in some cases, require vitrectomy (Hahn et al., 2015)
 - ▶ Post injection glaucoma: clogging of the trabecular meshwork (Wingard, et al, 2019)

Purpose

- ▶ To examine some potential risk factors of release of silicone oil droplets in anti- VEGF injections
 - ▶ compounding
 - ▶ injection techniques
 - ▶ drug

Methods

- ▶ Quantitative in-vitro study
- ▶ Three anti-VEGF agents (Bevacizumab, Ranibizumab and Aflibercept) + control (sterile water for injection)
- ▶ Compounding process:
 - ▶ the content of the industry vials was drawn into a 3 ml syringe ("base syringe" – BD and TERUMO)
 - ▶ compounded into the drug delivery syringe (BD 0.3ml Insulin Syringe).



Base syringe:

3 ml syringe

BD or TERUMO



Delivery syringe



BD Insulin 0.3 ml syringe
with needle 29 G ½ inch

Methods

- ▶ The contents were injected into amber glass vials (silicone-free)
- ▶ Four different techniques of injections:
 - ▶ Normal
 - ▶ Heavy
 - ▶ Agitation
 - ▶ Overfill

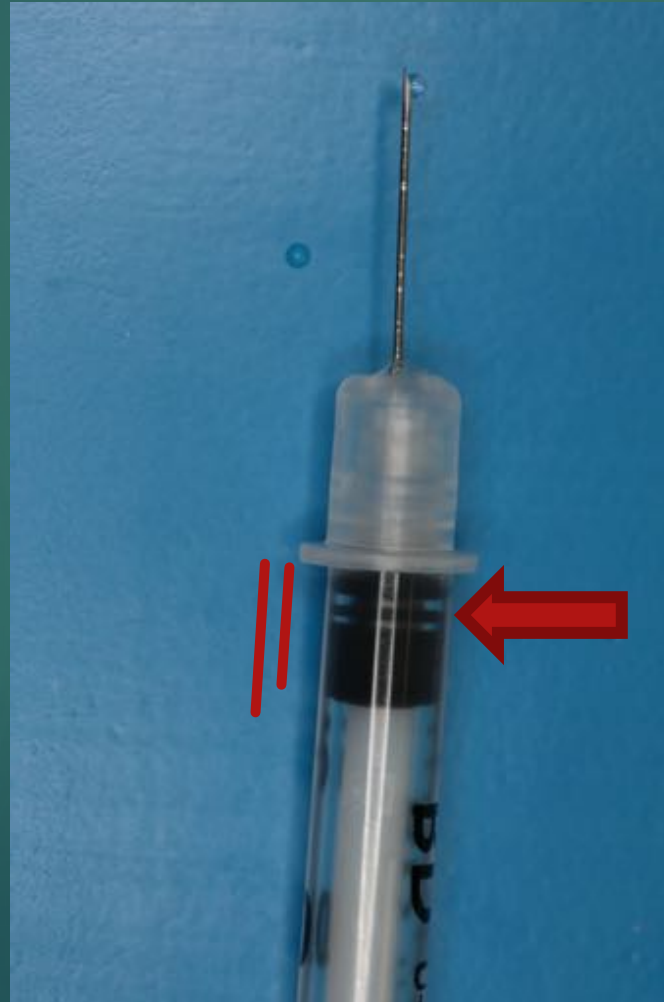


Methods: techniques

Normal:



Heavy:



Agitation:



Overfill:

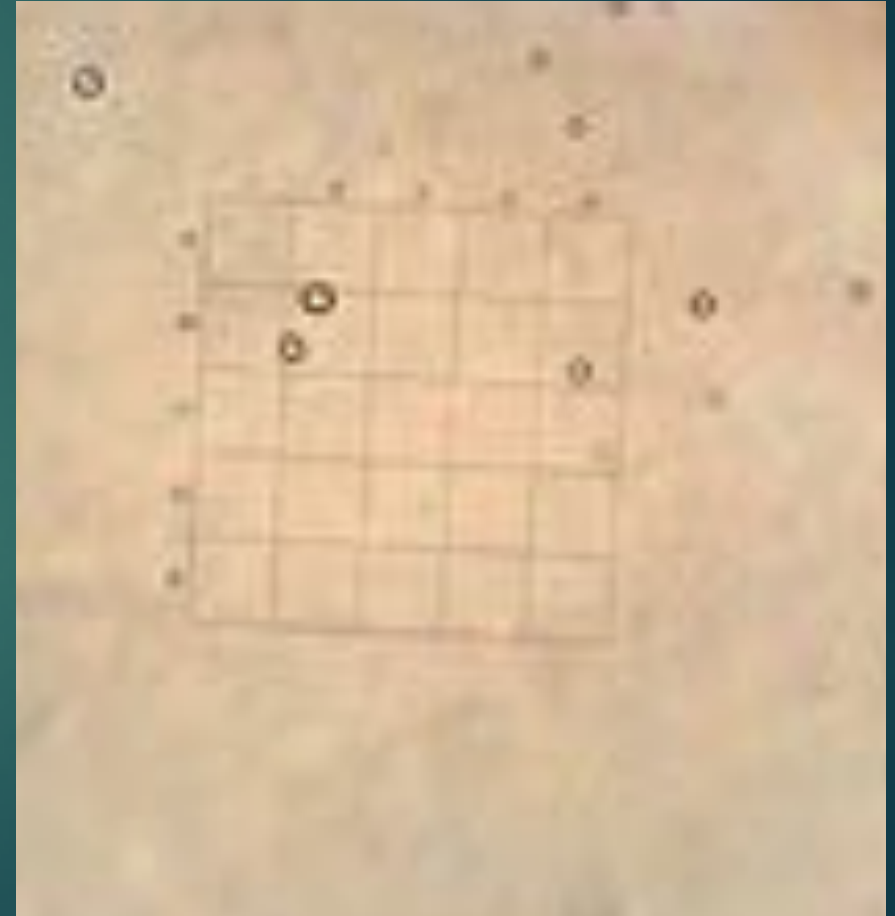
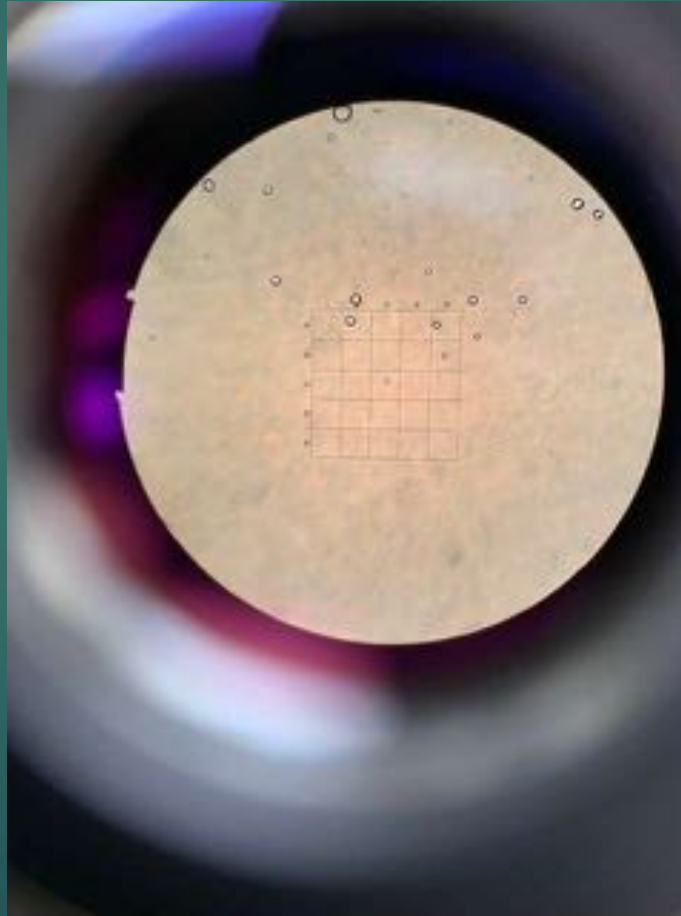
- Syringe prepared with .07 ml
- .02 ml is primed
- .05 ml is injected

Methods

- ▶ Content was examined for the presence and quantity of SiO droplets
- ▶ 100 x magnification with a Brightfield light microscope
- ▶ Hand tally counter was used to count the number of drops.
- ▶ Each vial was tested in triplicate ($3 \times 3\mu\text{L}$)



Methods



Rationale/Hypothesis

- ▶ Source of silicone oil droplets:
 - ▶ Base syringe (compounding)?
OR
 - ▶ Delivery syringe?
- ▶ Impact on the presence:
 - ▶ Technique?
OR
 - ▶ Drug?

Results

► Organization of trials

Syringe	Total of Trials
Delivery syringe (after compounding)	792
Base syringe only	36
Total	828

Drug	Total of Trials:
Aflibercept	228
Bevacizumab	246
Ranibizumab	108
Control	246
Total	828

Technique	Total of Trials:
normal	288
heavy	288
overfill	108
agitation	108
Total	828

Results

- ▶ Base syringe (3cc) for compounding:
 - ▶ TERUMO VS BD
 - ▶ By student's t-test, the when testing the base syringe alone, there was **no significant difference in the quantity of SiO oil found, $p=0.376$**



Base syringe:

3 ml syringe

BD or TERUMO

-> TEST FOR SiO Droplets

Results



BD Base syringe:



Delivery syringe

Terumo Base syringe:

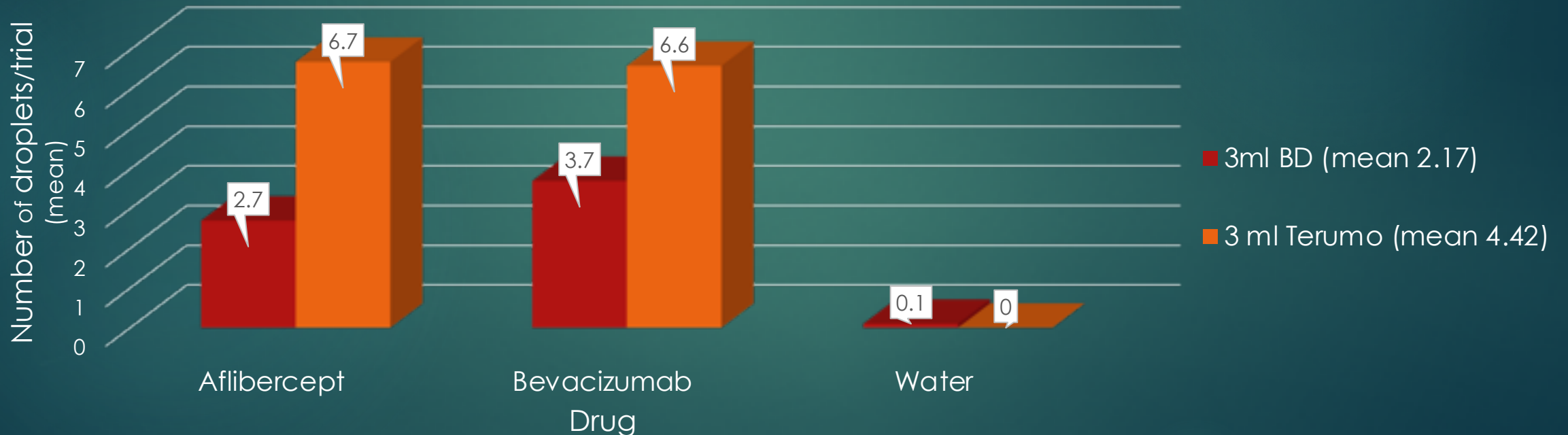


Delivery syringe

► Base syringe & Delivery syringe:

► TERUMO VS BD

Base syringe and drug

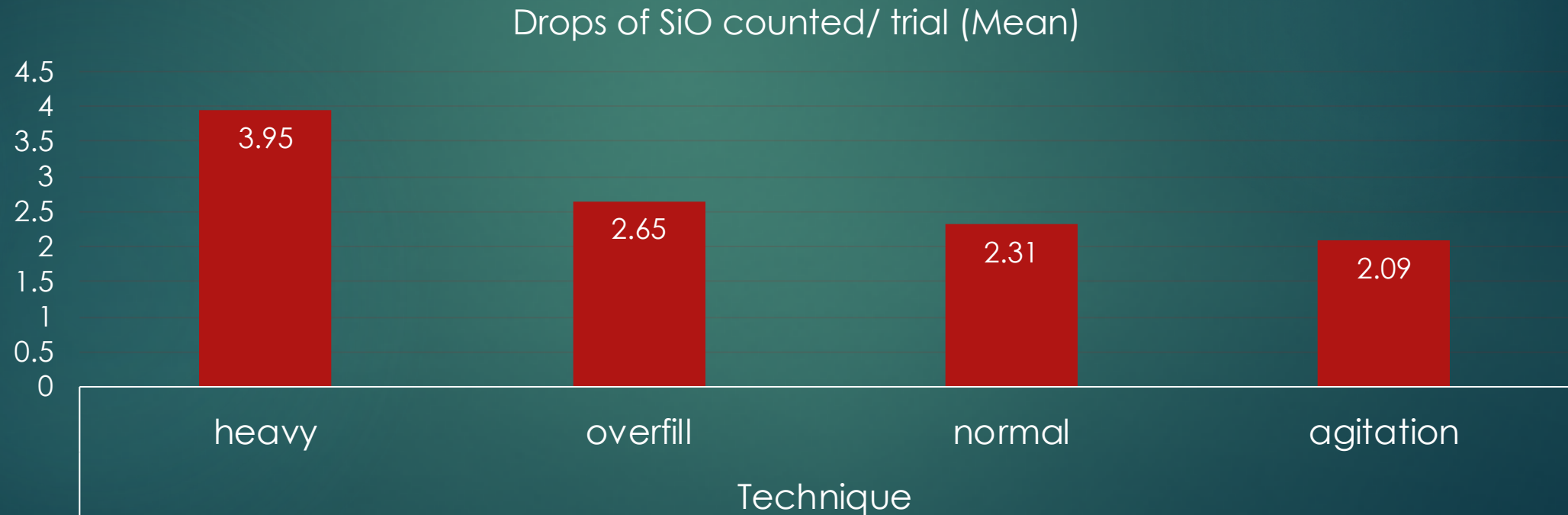


By Student's T test, there was a statistically significant difference between the quantity of SiO droplets between BD and Terumo base syringes, $p=0.05$

Results

► Technique

► Heavy vs normal vs agitation vs overfill

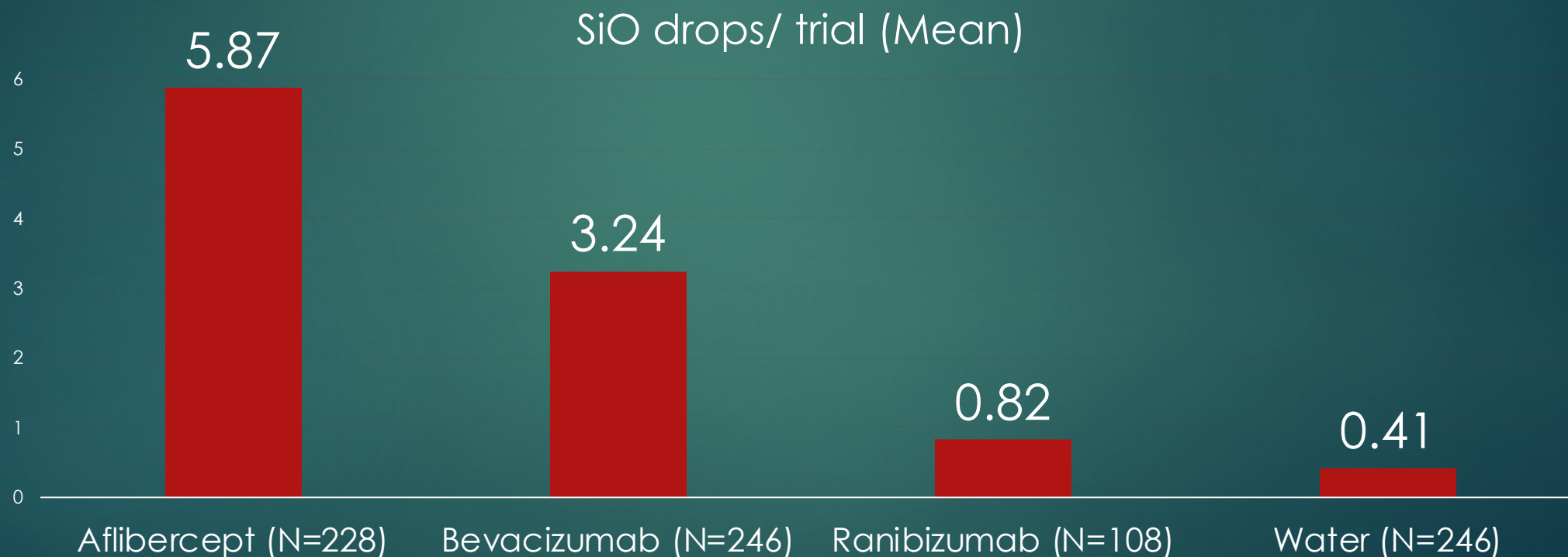


One way anova: there was no significant difference in quantity of SiO found between groups, $p > 0.05$ ($p = .189$);

Results

► Drug

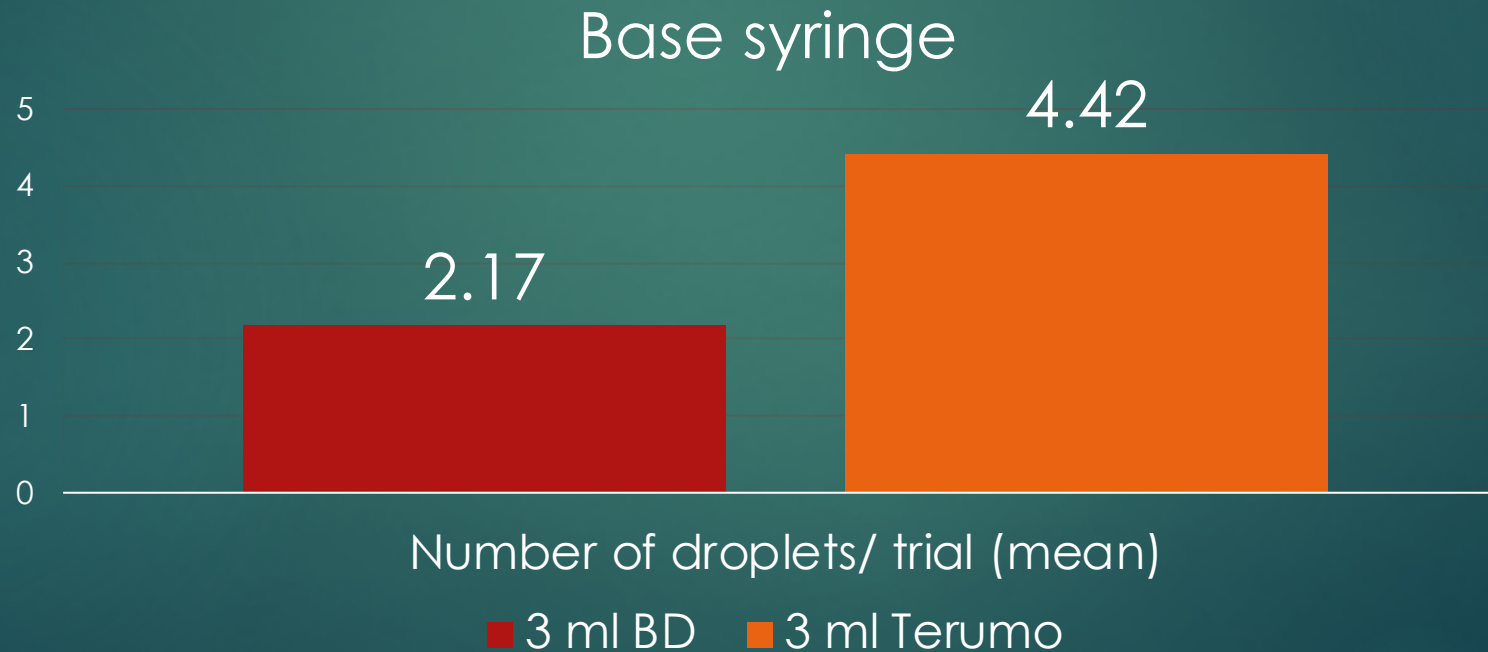
► Aflibercept vs Bevacizumab vs Ranibizumab vs Control (Water)



Conducted one -way ANOVA comparing quantity of SiO droplets (significant)

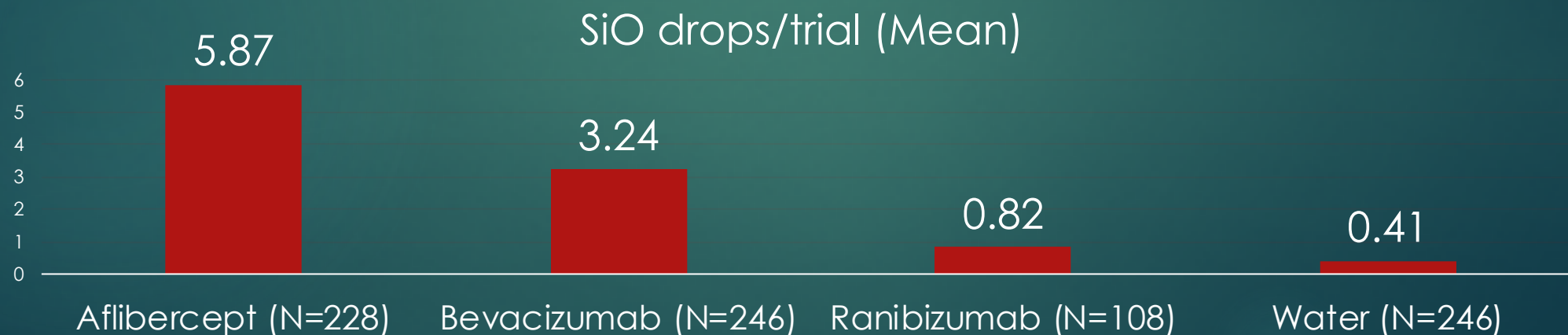
Conclusion

- Compounding processes can be a source of SiO droplets for anti-VEGF injections.



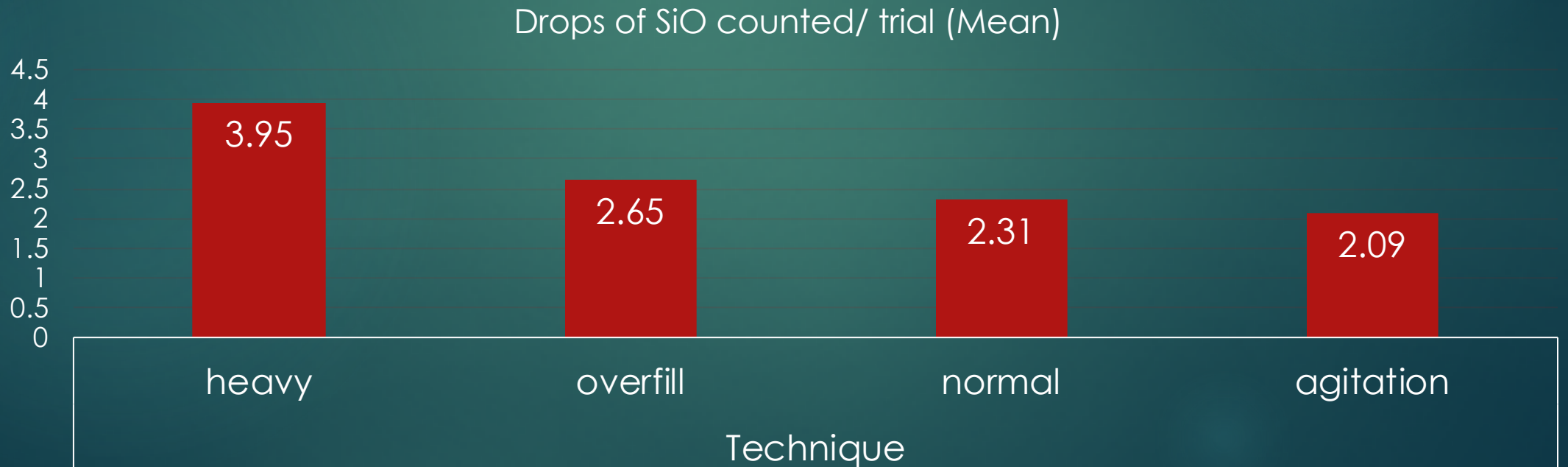
Conclusion

- ▶ Syringes containing anti-VEGF agents release more silicone oil droplets compared to syringes with control (water)
 - ▶ Suggesting a possible interaction between the anti-VEGF molecules and SiO.
 - ▶ Different between the 3 anti-VEGF agents studied.



Conclusion

- ▶ The “Heavy force” technique is associated with an increased number of SiO droplets per trial.
- ▶ Not statistically significant



Conclusion

- ▶ This study has also showed variability between insulin syringes of the same manufacturer
 - ▶ suggesting that the amount of SiO as lubricant in each syringe may be variable.

Technique	drops of SiO/ trial			
	N	Mean	Maximum	Minimum
Normal	288	2.31	50	0
Heavy	288	3.95	50	0
Overfill	108	2.65	31	0
Agitation	108	2.09	27	0

		Average SiO drops/trial (Range)
Drug	Aflibercept (N=228)	5.87 (0-50)
	Bevacizumab (N=246)	3.24 (0-50)
	Ranibizumab (N=108)	.82 (0-9)
	Water (N=246)	.41 (0-17)

Thank you

