

## INTRODUCTION

- Tuberculosis (TB) remains a worldwide health problem with 1.6 million deaths and 10.6 million infections in 2021. Patient compliance to available treatments is poor due to the long treatment times and severe side effects.<sup>1</sup>
- OHet72 (figure 1) is a novel compound with potent anti-TB activity and little to no side effects, but it has poor water solubility.
- Pulmonary administration of OHet72 nanocrystals (NCs) will deliver the drug to the main site of TB infection and will overcome the problem of solubility.<sup>2</sup>
- Administration of aerosols by nebulization offers several benefits, including the possibility of delivering large doses of drug directly to the lungs and it does not require patient breathing at maximum force or coordination of inhalation and aerosol generation.<sup>3</sup>
- The efficiency of commercially available nebulizers and the droplet size of the aerosol that they produce, are influenced by factors, such as: The make and model of the nebulizer as well as the volume and concentration of the drug.<sup>4</sup>
- In order to reach human alveoli droplet size must be under 5  $\mu\text{m}$  and under 1  $\mu\text{m}$  for mice. Thus, the droplet size of the emitted aerosol will determine the efficacy of the proposed treatment.<sup>4</sup>

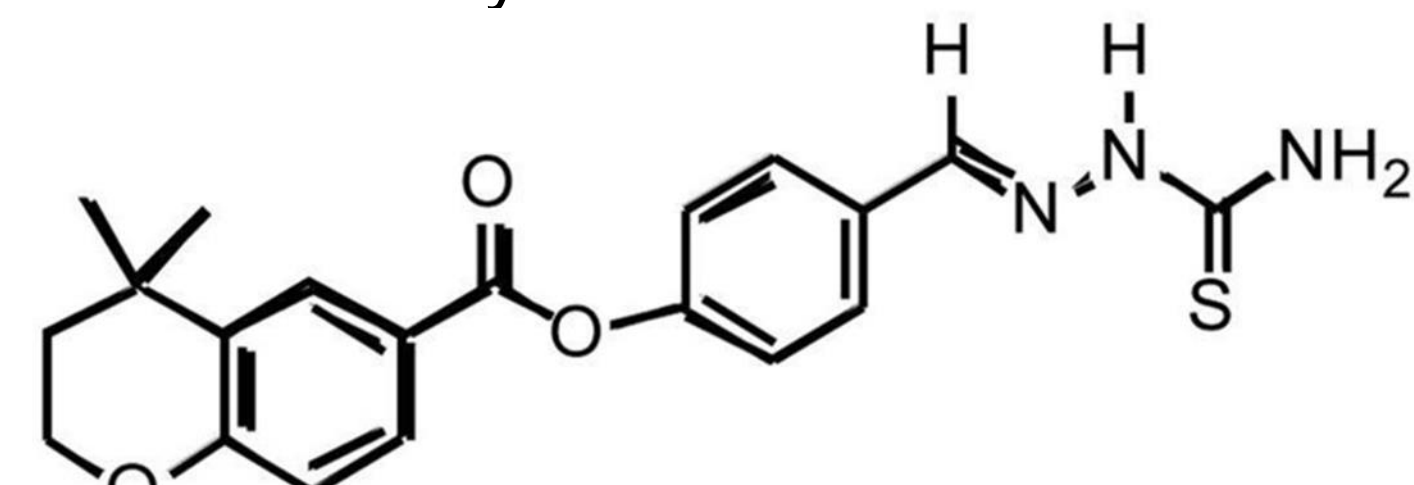


Figure 1: Structure of OHet72

## PURPOSE

- Determine the efficiency of different nebulizers to generate aerosols from OHet72 nanosuspensions to treat TB in a mouse model.

## METHODS

- Two air jet nebulizers (Hudson UP-DRAFT II® OPTI-NEB® and PARI LC STAR® nebulizer with a Vios Pro compressor) and the Aeroneb® Lab ultrasonic nebulizer were first evaluated using a model solution (sodium fluorescein (NaF) 3 mg/mL in saline).
- The aerosol performance was assessed in terms of their mean mass aerodynamic diameter (MMAD), geometric standard deviation (GSD) and fine particle fraction (FPF) using a New Generation Impactor (NGI) at a 15 L/min flow rate and 15 minutes run time.
- OHet72 NCs were prepared by the bottom-up solvent-antisolvent precipitation method (Figure 2). Size and morphology was determined using Scanning Electron Microscopy (SEM) and ImageJ software (NIH).
- OHet72 NCs were suspended in saline (3mg/mL) in order to determine their aerosol performance in the selected nebulizer as described above.

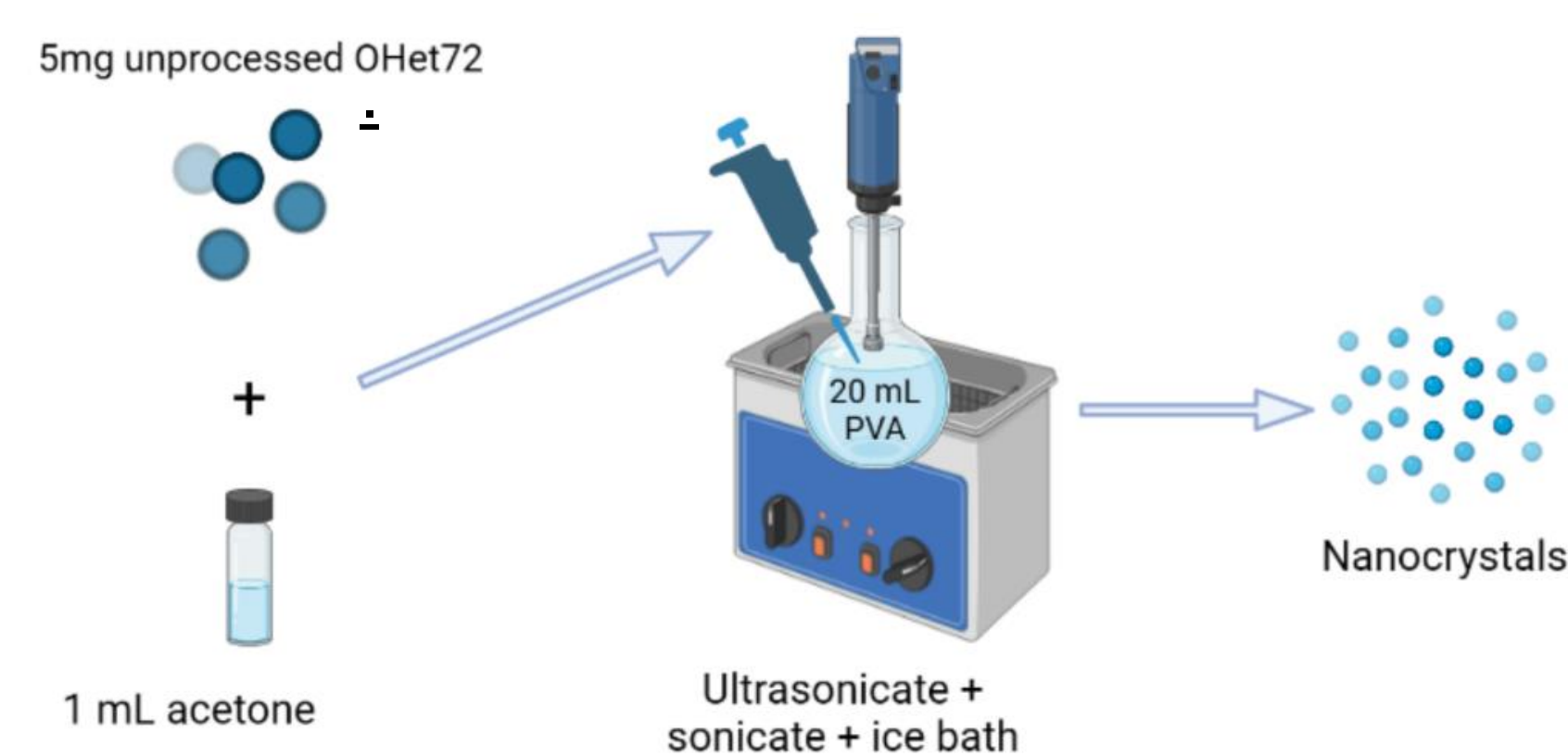


Figure 2: Preparation procedure for OHet72 NCs.

## RESULTS

### Aerosol Performance of Sodium Fluorescein in the Nebulizers tested

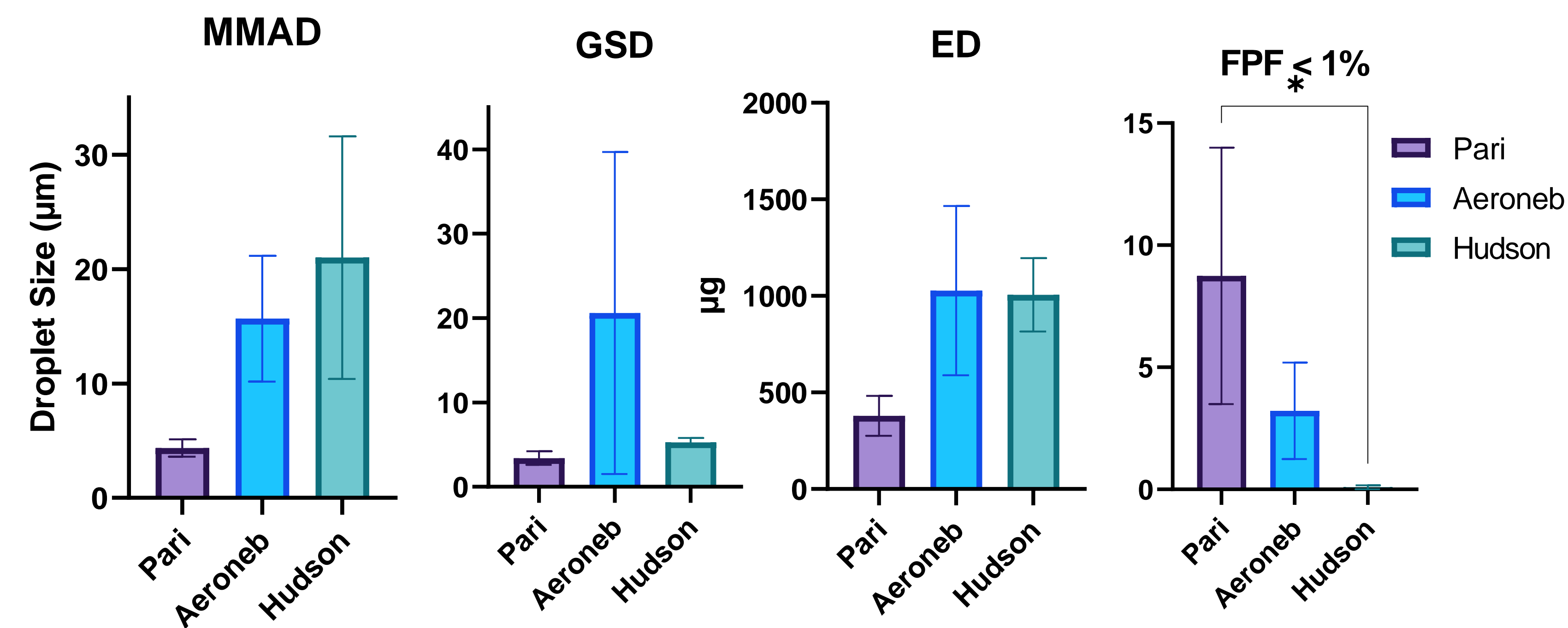


Figure 3: Mean  $\pm$  standard deviation of Mean Mass Aerodynamic Diameter (MMAD), Geometric Standard Deviation (GSD), Emitted Dose (ED), and Fine Particle Fraction less than 1% (FPF < 1%).

Table 1: Cut-off diameters for each stage of the NGI operated at 15 L/min.

Stage	Cutoff Diameter ( $\mu\text{m}$ )
1	14.1
2	8.61
3	5.39
4	3.3
5	2.08
6	1.36
7 + MOC	0.98

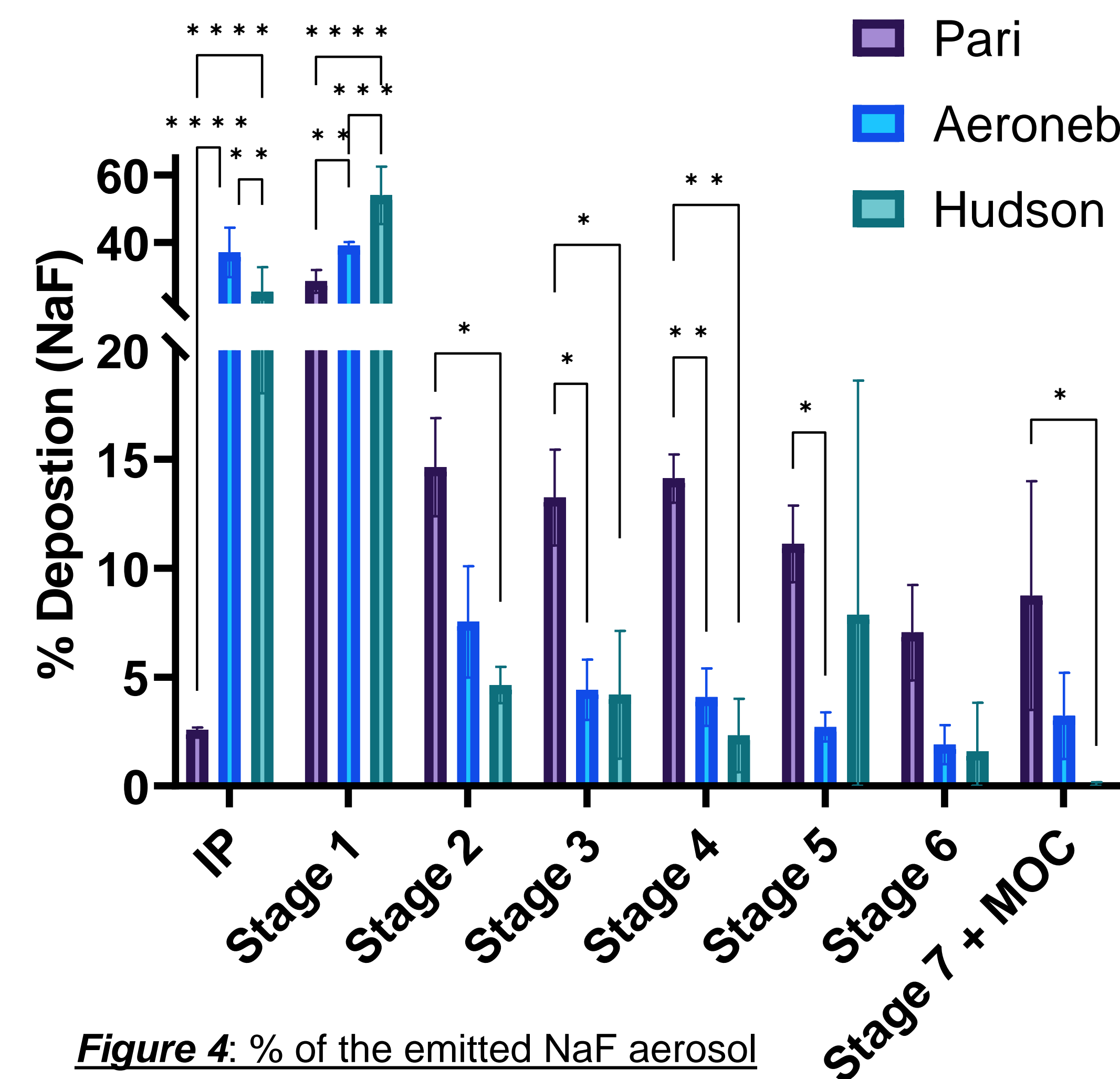


Figure 4: % of the emitted NaF aerosol dose deposited in each stage of the NGI.

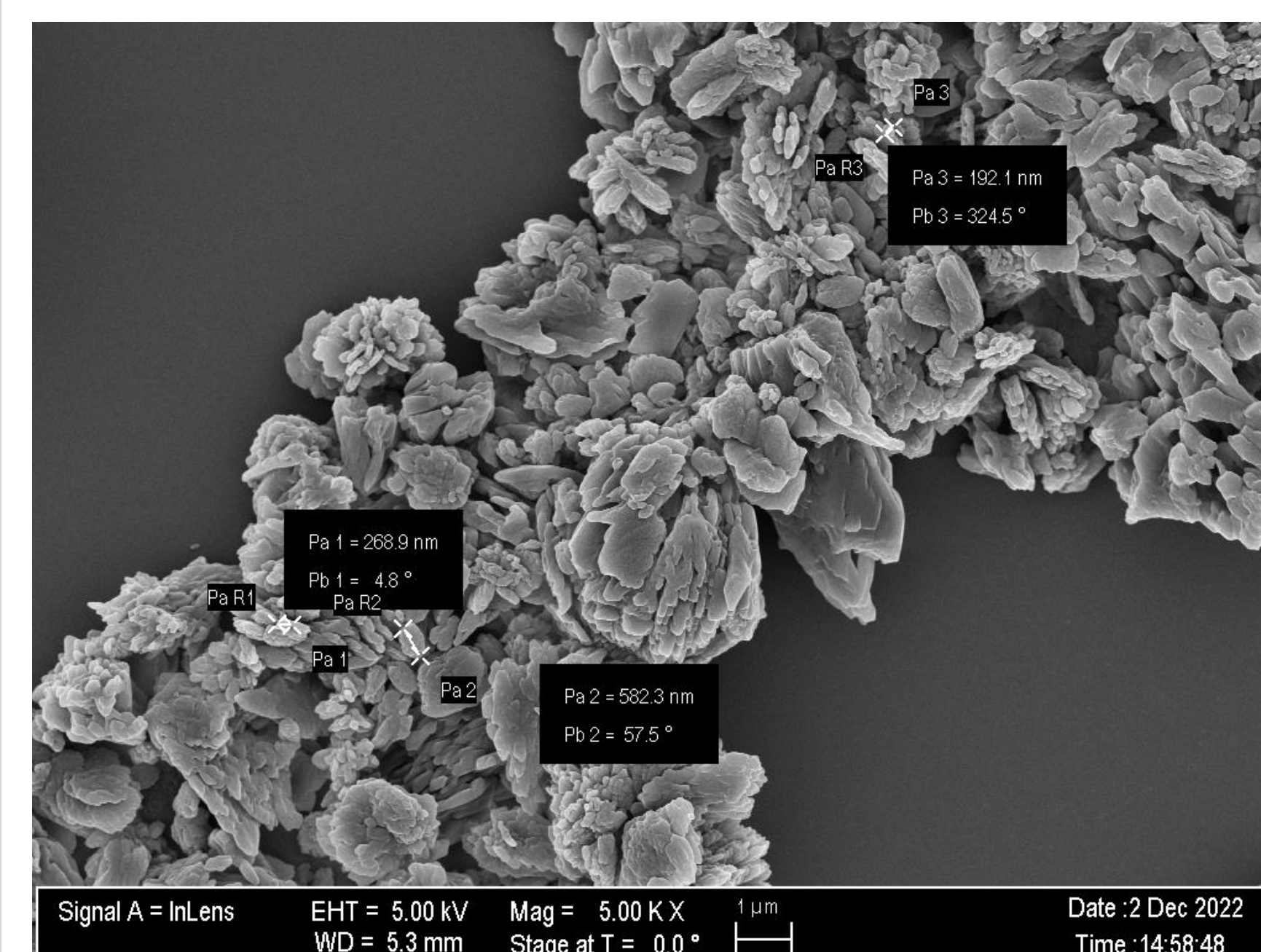


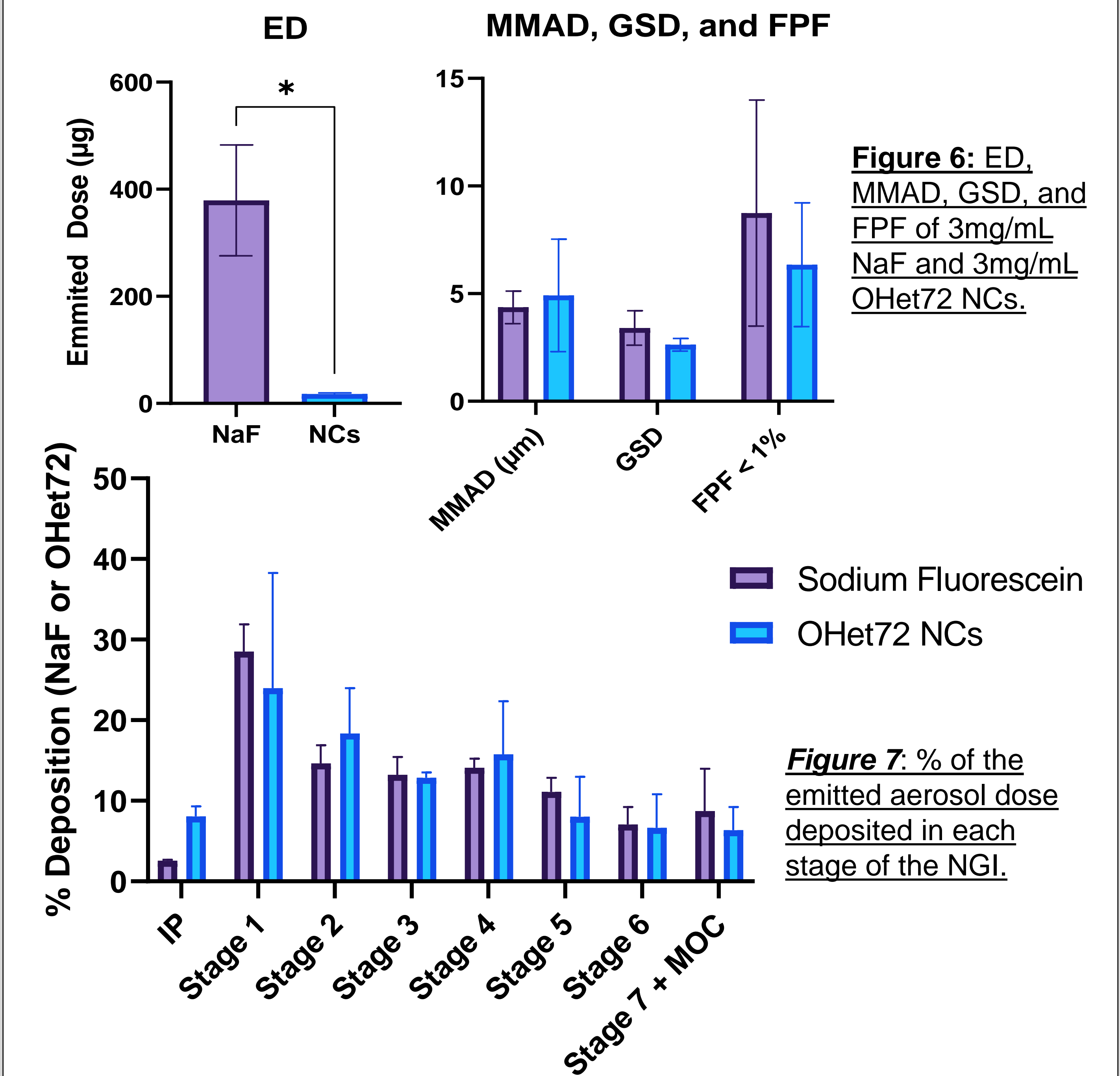
Figure 5: SEM image of OHet72 NCs

Table 2: Geometric diameter ( $d_g$ ) and geometric standard deviation (GSD) of OHet72 NCs.

Geometric Diameter ( $\mu\text{m}$ )	GSD ( $\sqrt{84/16}$ )
Length: 0.245	Length: 2.96
Width: 0.235	Widths: 1.98

## RESULTS

### Comparison of Aerosol Performance: Sodium Fluorescein vs. OHet72 NCs



## CONCLUSION

- The PARI LC STAR® nebulizer generated aerosols with smaller droplets and a more homogenous size distribution than the Hudson UP-DRAFT II® OPTI-NEB® nebulizer and Aeroneb® Lab nebulizer; thus, would be more suitable to use in efficacy studies in TB infected mice.

## REFERENCES

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