

DECOUPLING POWDER PROPERTIES FROM REGIONAL DEPOSITION IN AN INTRANASAL DELIVERY SYSTEM

Influence of Particle Size and Flow Dynamics on Plume Geometry

Zachary Warnken¹ • Matthew Herpin² • Timothy Sullivan³

¹Via Therapeutics, Austin, TX | ²The University of Texas at Austin, College of Pharmacy, Austin, TX | ³Zeteco Biomedical LLC, Austin, TX



POWDER PROPERTIES RESHAPED THE PLUME — NOT THE REGIONAL DEPOSITION PATTERN

Across five formulations, plume angle ranged 11.1°–19.2° (~73%); regional deposition remained closely aligned in the two formulations evaluated in the nasal cast.

BACKGROUND / WHY IT MATTERS

For liquid nasal sprays, plume geometry is widely considered an important factor influencing deposition behavior, although its relative contribution depends on device design and use conditions. For nasal powders, the influence of particle size and flow properties on plume formation and regional deposition is less well characterized. Understanding whether formulation-driven plume differences translate into regional deposition changes is important for defining formulation design space and relevant critical quality attributes (CQAs).

OBJECTIVE

Evaluate whether variation in powder particle size and flow properties influences plume geometry, and determine whether those differences affect regional nasal deposition when delivered using the CygnusMR™ intranasal powder system.

STUDY DESIGN & METHODS

Five naloxone HCl powder formulations

- <38 µm sieved fraction of neat API
- >38 µm sieved fraction of neat API
- Wet granulation: naloxone HCl + Avicel PH-102; HPMC binder (mortar/pestle)
- Spray-dried naloxone HCl (Pilotech YC-501; two-fluid nozzle)
- Spray-dried naloxone HCl:HPMC E5 (4:1; Pilotech YC-501)

Characterization and performance testing

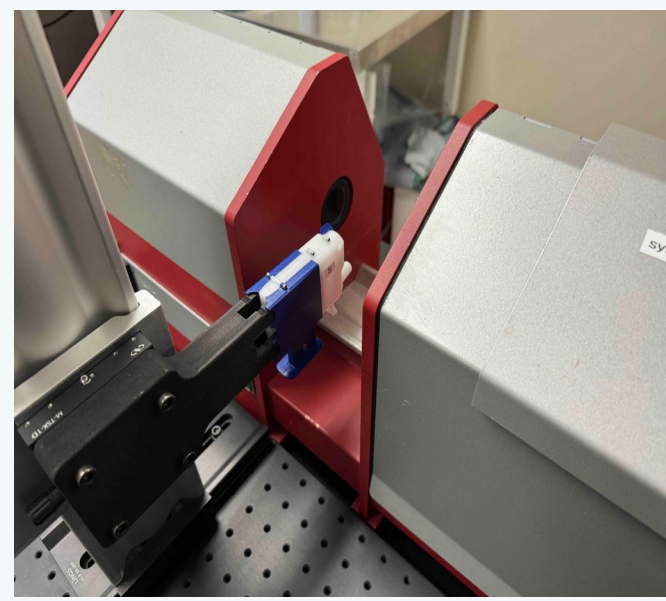
- Angle of repose (AOR) and bulk density
- RODOS laser diffraction: emitted Dv50 and dispersibility
- Photron high-speed imaging: plume cone angle
- CT-derived 3D nasal cast: regional recovery by mass balance

Replicates: AOR n=3; plume angle n=2–3/formulation; deposition n=5/formulation. Dv50 and bulk density were single measurements.

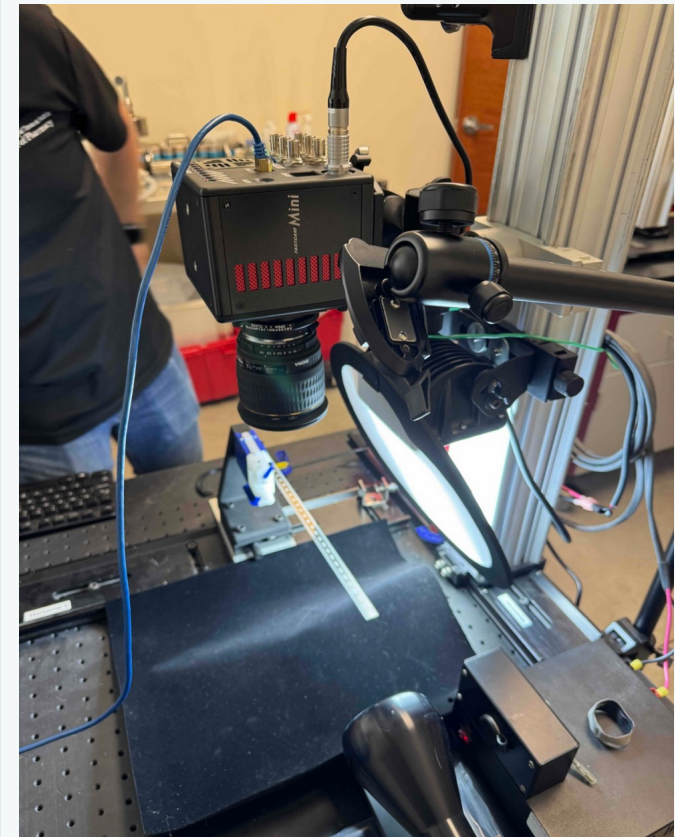
DEVICE & INSTRUMENTATION



CygnusMR™ device



Sympatec / RODOS laser diffraction



Photron high-speed plume imaging

FIGURE 1A — PARTICLE SIZE vs PLUME GEOMETRY

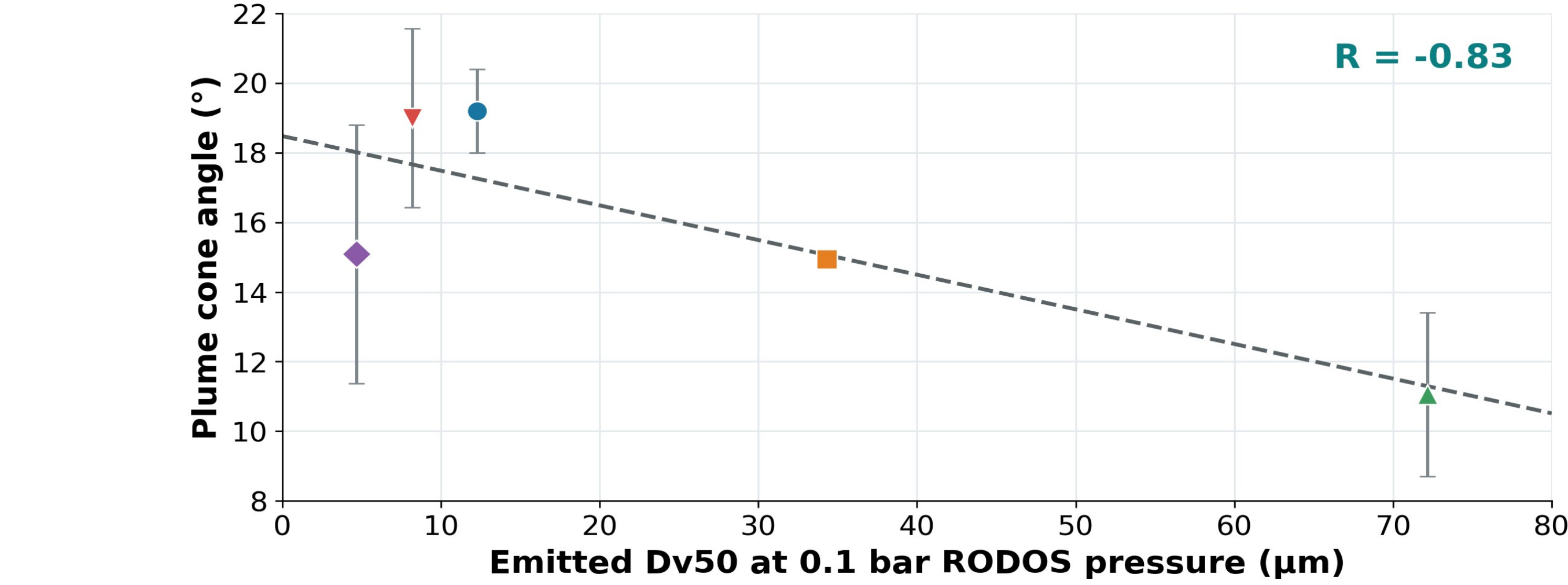
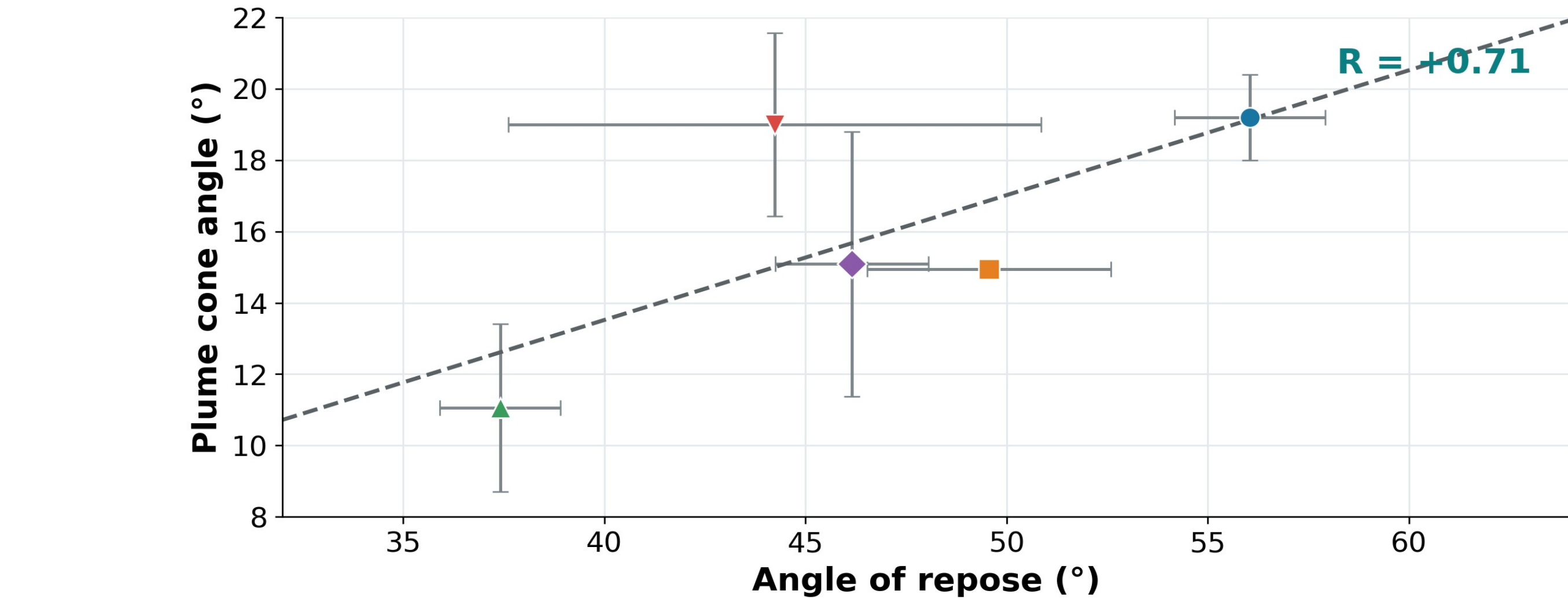


FIGURE 1B — FLOW / COHESIVITY vs PLUME GEOMETRY



FORMULATION CHARACTERIZATION SUMMARY

Formulation	AOR (°) mean ± SD	Bulk density (g/mL)	Dv50 (µm)	Plume angle (°) mean ± SD
<38 µm sieved API	56.0 ± 1.9	0.225	12.27	19.2 ± 1.2
>38 µm sieved API	49.6 ± 3.0	0.384	34.31	14.9 ± 0.1
Wet granulation	37.4 ± 1.5	0.434	72.18	11.1 ± 2.3
Spray-dried naloxone	46.2 ± 1.9	0.148	4.68	15.1 ± 3.7
Spray-dried naloxone:HPMC (4:1)	44.2 ± 6.6	0.172	8.19	19.0 ± 2.6

Bulk density and Dv50 are shown descriptively (single measurement per formulation).

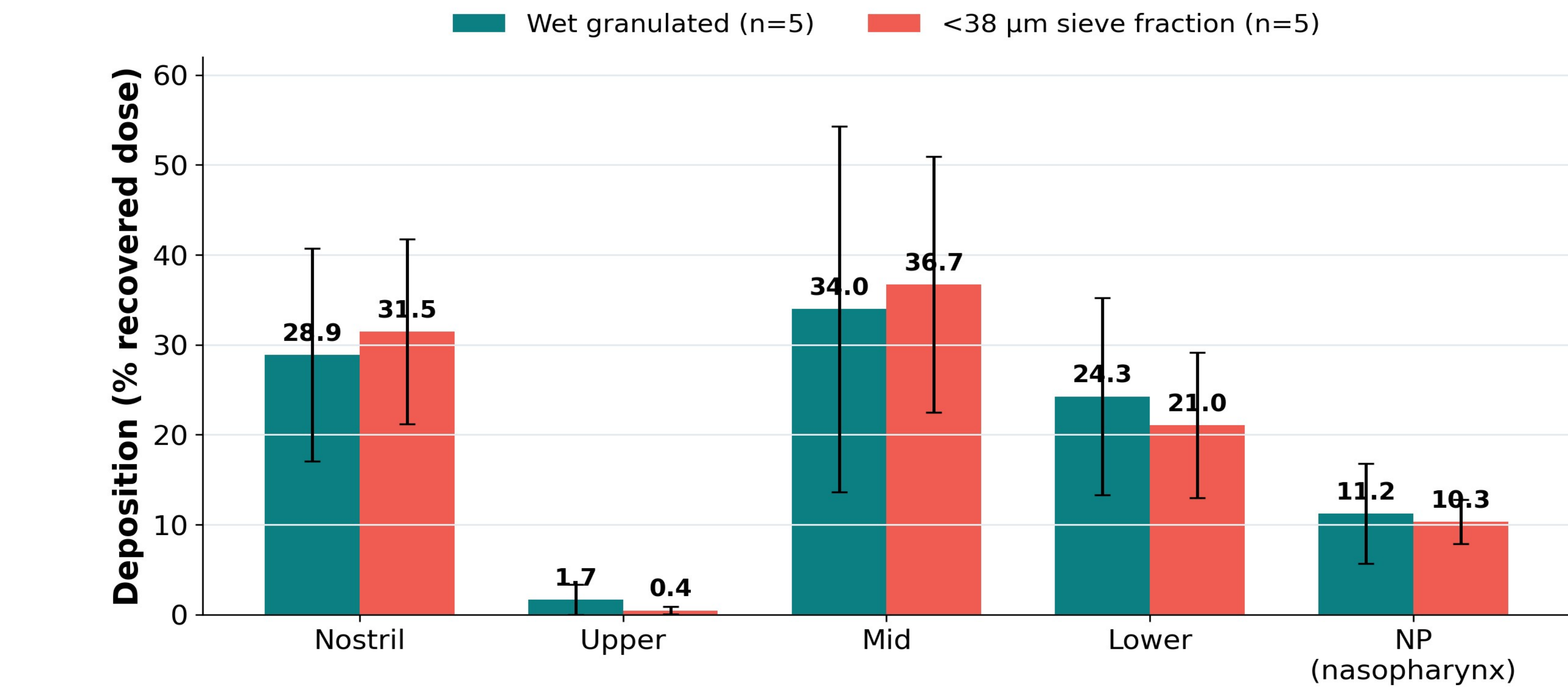
OBSERVATION

Plume cone angle spanned 11.1° → 19.2° (~73% range) across the five powder architectures.

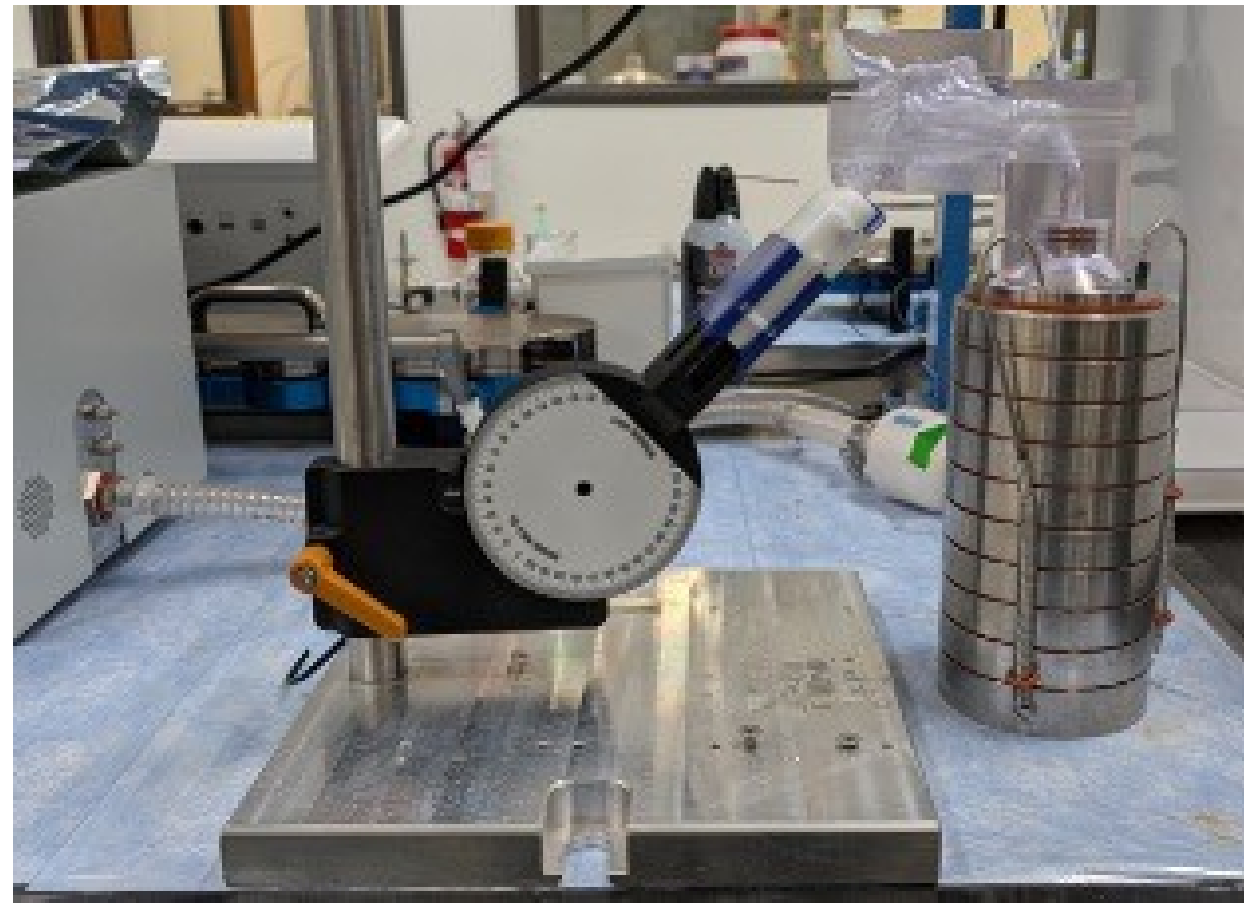
Strongest formulation-level associations: emitted Dv50 (R = -0.83) and AOR (R = +0.71).

FIGURE 2 — REGIONAL NASAL DEPOSITION

Mean recovered dose by anatomical region; wet-granulated vs <38 µm sieve-fraction formulations



NASAL CAST DEPOSITION SETUP



CygnusMR™ device aligned to the CT-derived nasal cast mounted over an Andersen cascade impactor. The cast was pre-coated with 1.5% polysorbate in isopropanol and allowed to dry before testing.

INTERPRETATION / ENGINEERING IMPLICATIONS

- Large plume-angle differences did not produce a clear shift in regional deposition in the two formulations evaluated in the nasal cast.
- Device-driven dispersion may buffer formulation-dependent variability within this operating range, reducing sensitivity of regional deposition to powder architecture.
- Plume geometry should not be treated as a stand-alone surrogate for deposition without considering device mechanics, emitted particle properties, and the relevant operating envelope.
- Additional formulations and broader plume regimes are needed to define the limits of this apparent decoupling and establish predictive relationships to in vivo performance.

CONCLUSIONS

1 Powder properties affected plume formation

Particle size and powder flow/cohesivity were associated with substantial differences in plume cone angle across five naloxone HCl formulations.

2 Regional deposition was comparatively robust

For wet-granulated and <38 µm formulations, the recovered-dose distribution across nostril, upper, mid, lower, and nasopharyngeal regions remained closely aligned.

3 Formulation–device interactions define the design space

Within the evaluated range, plume geometry alone was not the primary determinant of regional deposition. The result supports further work to map the edges of the CygnusMR™ operating envelope.