

Initial deposition features (t=0h)	Intranasal liquid aspiration (INLA)	Intratracheal Liquid Instillation (ITLI)	ventilator-assisted aerosol delivery (VAAD)	nose-only aerosol inhalation (NOAI)
Type of application of NP suspension	bulk liquid	bulk liquid	liquid aerosol	liquid aerosol (dried)
Volume-median aerodynamic diameter of inhaled aerosol (μm)	N/A	N/A	2.8 ± 1.58*	0.7±0.1**
Invested liquid volume (μl)	50	50	20	190
Invested dose (μg)	34.7	25	166.7	475
Deposited dose fraction (lung + trachea)	28.1% ± 16.6%	59.2% ± 14.47%	4.24 % ± 1.58 %	0.19% ± 0.02%
Deposited dose (lung + trachea) (μg)	9.7 ± 5.76	14.1 ± 3.68	7.06 ± 2.63	0.91 ± 0.12
Deposited dose (lung without trachea) (μg)	9.7 ± 5.76	14.1 ± 3.68	4.50 ± 1.58***	0.91 ± 0.12
Homogeneity of depo. pattern	patchy	patchy	homogeneous	homogeneous
Central/peripheral dose (C/P) ratio (uniform: C/P=1)	3.79 ± 0.72	2.28 ± 0.27	1.37 ± 0.13	1.32 ± 0.14
Bronchial/acinar dose ratio	0.49 ± 0.14	0.23 ± 0.05	0.12 ± 0.02	0.08 ± 0.01
Bronchial deposited fraction	0.32 ± 0.06	0.18 ± 0.03	0.11 ± 0.02	0.08 ± 0.01
Acinar deposited fraction	0.67 ± 0.07	0.81 ± 0.03	0.89 ± 0.02	0.92 ± 0.01
Apparent NP volume/dose (μm ³ /μg) in bronchi	1.77E+07 ± 3.85E+06	4.17E+07 ± 2.08E+07	5.28E+07 ± 1.90E+07	3.86E+08 ± 3.53E+08
Apparent NP volume/dose (μm ³ /μg) in acini	4.92E+07 ± 1.40E+07	1.14E+08 ± 4.32E+07	1.60E+08 ± 4.82E+07	1.27E+09 ± 5.63E+08
Apparent NP-covered volume fraction in bronchi	0.12 ± 0.05	0.19 ± 0.04	0.05 ± 0.02	0.03 ± 0.01
Apparent NP-covered volume fraction in acini	0.07 ± 0.02	0.18 ± 0.04	0.13 ± 0.03	0.14 ± 0.09
Upper/lower half of lung	preferential in upper/central	preferential in upper/central	uniform	uniform
bronchial (dose/area): central or peripheral preference	High deposition in secondary bronchi; central bronchiolar deposition in upper part of the lung	central bronchioles	equal deposition in central to peripheral (bronchioles)	equal deposition in central to peripheral (bronchioles)
inter-acinar (dose per area): central or peripheral preference	Central acini received most of NPs; peripheral acini had little/no particles	central acinar received most of NPs	Equal central to peripheral acinar deposition	Equal central to peripheral acinar deposition
intra-acinar (dose per area): proximal or distal preference	highly proximal acinar region (PAR)	highly PAR	slightly PAR	relatively uniform
not/poorly exposed lung regions	peripheral acini and distal acinar region (DAR)	A few peripheral acini and DAR of peripheral acini	DAR of all acini	slight DAR of all acini
Additional features	little trachea deposition	little trachea deposition	hot spot trachea (20-40% of total deposition)	little trachea deposition

Longitudinal NP deposition features (t=2h, 24h, 14d)				
inter-acinar Biokinetics (t=2h, 24h, 14w)	no data available	No NP-transfer bewteen acini	No NP-transfer bewteen acini	no data available
intra-acinar Biokinetics (t=2h, 24h, 14w)		NP transport in PAR and DAR	NP transport in PAR and DAR	
Bronchial deposited fraction_2h		0.11 ± 0.01	0.11 ± 0.01	
Bronchial deposited fraction_24h		0.11 ± 0.04	0.10 ± 0.03	
Bronchial deposited fraction_14d		0.07 ± 0.01	0.06 ± 0.01	
Acinar deposited fraction_2h		0.88 ± 0.01	0.88 ± 0.01	
Acinar deposited fraction_24h		0.89 ± 0.04	0.89 ± 0.02	
Acinar deposited fraction_14d		0.92 ± 0.01	0.93± 0.01	
Retained dose fraction_2h		54.35% ± 3.88%	2.35% ± 0.40%	
Retained dose fraction_24h		57.60% ± 1.56%	2.86% ± 0.83%	
Retained dose fraction_14d		14.64% ± 3.14%	0.84% ± 0.11%	

* The aerodynamic diameter of doplets of the melamin NP suspension was measured in dedicated experiments. There an ionic liquid-water mixture (instead of melamin NP suspension) was nebulized. After drying of these droplets into a spherical residue particle (ionic non-volatile liquid) we measured the particle diameter (using a scanning mobility particle sizer) and inferred the diameter of the original aerosol drop entering the trachea by accounting for the known water-ionic liquid mixing ratio (50:1).

** Derived from the volume-weighted median equivalent mobility diameter (measured with scanning mobility particle sizer (SMPS)) and the density of melamin particles = 1.51 g/cm³.

*** Here only the lung deposited dose was displayed, the lung deposited dose = 166.7*4.24*0.60. Since ca 40% of dose is deposited to the lung trachea reported by Yang et al. Schmid, 2023, other administrations had very little NP trachea deposition