# Analysis of Anderson Cascade Impactor Performance with Modified 3D Printed Induction Port

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## Abstract

**Background:** The Anderson Cascade Impactor (ACI) is a commonly used instrument for assessing the aerodynamic parameters of inhalable microparticles. However, relatively little is known as to whether findings from ACI studies translate *in-vivo*. In this study, we investigate the effect of a 3D printed human trachea as a modified induction port (IP) on the particle size distribution and aerodynamic parameters of model maltodextrin-polyvinylpyrrolidone (M-PVP) microparticles.

**Methods:**M-PVP microparticles were produced using 5% (w/v) maltodextrin, 5% (w/v) PVP with 0.05% (w/v) fluorescein and spray dried using a Büchi B-191 mini spray dryer (Büchi, Flawil, Switzerland). A standard IP was printed according to specifications outlined in USP <601> using a German RepRap X400 3D printer (German RepRap GmbH) and was used as a control. A human trachea replicate was modeled from reconstructed CT images obtained from the National Biomedical Image Archive and printed. Three separate ACI experiments were conducted to compare the standard USP IP, the printed IP and the trachea. Statistical analysis of ACI results included one-way ANOVA followed by Bonferroni adjusted $t$-test to assess differences between the three IPs.

**Results:** ANOVA of relative mass fraction across each stage revealed significant differences between the throat ($p = 1.42 \times 10^{-8}$), preseparator ($p = 1.53 \times 10^{-5}$), stage 0 ($p = 5.04 \times 10^{-6}$), stage 1 ($p = 0.01$) and stage 6 ($p = 0.02$). Subsequent $t$-test reveals significantly higher mass fraction in the trachea IP compared to the PLA IP ($p = 0.00083$) as well as the standard metal IP ($p = 1.3 \times 10^{-5}$). No significant differences were observed in the fine particle fraction (FPF) among the three IPs. Additionally, no statistically significant difference in mass median aerodynamic diameter (MMAD) or geometric standard deviation (GSD) was observed among the three induction ports.

**Conclusions:** Particle retention in the trachea IP resulted in significantly decreased particle accumulation in the preseparator however no significant difference in MMAD, GSD or FPF of the particles was observed.

## Objective

The aim of this study was to determine the effect of altered ACI IP geometry on aerodynamic and size distribution parameters of model maltodextrin particles. Specifically, we were interested in determining how the trachea influences these properties and how this may influence drug delivery with dry powder inhalers.

## Methods

**Particle formation:** Microparticles were produced using 5% (w/v) maltodextrin, 5% (w/v) PVP with 0.05% (w/v) fluorescein as proposed by Lamprecht and Ali [1]. The particles were spray dried using a Büchi B-191 mini spray dryer (Büchi, Flawil, Switzerland). The spray dry parameters can be seen in Table 1

## Methods continued

| Parameter | Value |
|---|---|
| Inlet temp. | $110^oC$ |
| Outlet temp. | $80^oC$ |
| Aspirator | 85% |
| Air flow | 750 |
| Feed rate | 3% (1 mL/min) |

Figure 1 : Spray dry parameters used to formulate microparticles.

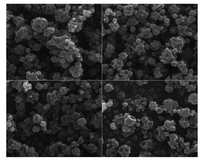

Figure 2 : SEM of maltodextrin-PVP (5:5) microparticles.

**PLA induction port:** To test the effect of the printer polymer (PLA) on the aerodynamic/size parameters of the particles we built a PLA IP based on the dimensions specified in USP <601> [2]. The IP was printed using the German RepRap X400 3D printer (German RepRap GmbH) Figure 3

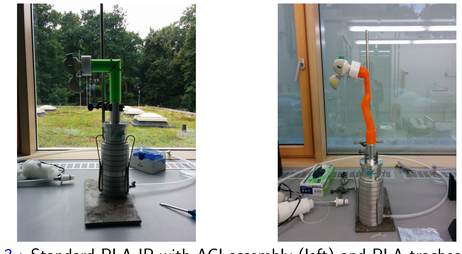

Figure 3 : Standard PLA IP with ACI assembly (left) and PLA trachea IP (right) with ACI assembly.

**PLA trachea induction port:** The trachea IP was reconstructed using CT images obtained from the National Biomedical Image Archive and printed using a German RepRap X400 3D printer with PLA filament (Figure 3).
**ACI analysis:** A total of six ACI runs were conducted for each of the IPs. The inspiratory flow rate was set to $28.40 \pm 0.2 L/min$ with a mean capsule load of $14.74 \pm 0.83 mg$ of microparticles. The ACI parameters can be seen in Table 1.

| IP type | Flow rate (L/min) | Capsule load (mg) |
|---|---|---|
| Standard metal | 28.28 ± 0.1 | 14.47 ± 1.4 |
| Standard PLA | 28.64 ± 0.12 | 14.6 ± 0.44 |
| Trachea PLA | 28.28 ± 0.06 | 15.17 ± 0.45 |

Table 1 : ACI parameters used to compare the three IPs (error is reported as standard deviation).

## Methods continued

**Statistical analysis:** Statistical analysis included one-way ANOVA followed by Bonferroni adjusted $t$-test with a family error rate of 5%. All stats were completed using R v.3.2.1.

## Results

The relative stage mass for each of the IPs can be seen in Figure 4.

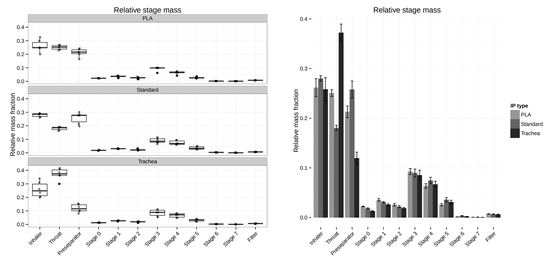


Figure 4 : Relative stage mass for each IP obtained from ACI experiments. Error bars report SE.

| Stage | F-value | $p$-value |
|---|---|---|
| Throat | 75.96 | $1.42x10^{-8}$ |
| Preseparator | 25.39 | $1.53x10^{-5}$ |
| Stage 0 | 30.65 | $5.04x10^{-6}$ |
| Stage 1 | 6.09 | 0.01 |
| Stage 6 | 5.10 | 0.02 |

Table 2 : Statistically significant results from ANOVA of relative stage mass across each of the induction ports.

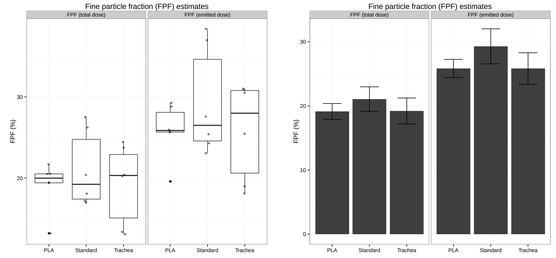


Figure 5 : Fine particle fractions for the three IPs. Error bars report SE.

## Results continued

MMAD and GSD for each of the IPs can be seen in Figure 6.

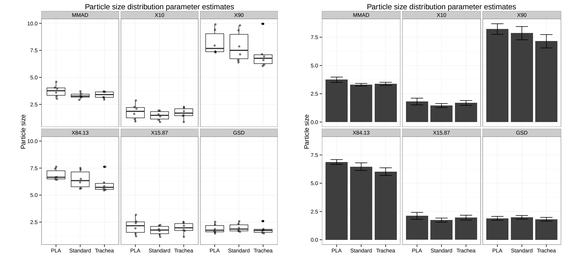


Figure 6 : GSD and MMAD determined for each of the IPs. Error bars report SE.

## Discussion

Significantly higher relative mass fraction was observed in the trachea IP compared to both the PLA IP and the standard IP. It was observed that higher relative mass fraction retained in the IP resulted in lower mass fraction being collected in the preseparator. This seems to suggest that agglomerates that would normally settle in the preseparator are settling in the IP instead. In spite of these findings, no statistically significant difference in FPF, MMAD, or GSD was observed suggesting that the process governing the retention of particles in the IP is not biased towards a particular size.

## Conclusion

Alteration of the ACI IP to simulate the anatomy of the human trachea had little effect on the aerodynamic and size parameters of the model microparticles.

## References

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