Investigating the Impact of Device Positioning on the Nasal Regional Deposition

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Key Message

The insertion angle and depth of a nasal drug product in the nose has a significant impact on the nasal regional deposition in a validated male nasal cast model.

Introduction

The nasal cavity provides an encouraging drug delivering route for novel therapies including vaccination, nose-to-brain delivery and non-invasive systemic delivery [1,2,3].

• Clinically relevant validated nasal cast models may provide useful insights into the regional deposition of nasal products which can impact the efficacy and safety of a nasal drug product [4].

• Objective: the impact of the device positioning on nasal regional deposition is evaluated by fixing the position of the nasal spray at different insertion angles / depths and evaluating the regional deposition in a validated nasal cast model.

Experimental Methods

• A jet-like nasal product with a small spray angle targeting a focused olfactory region deposition was explored. Nasal unit dose powder devices (Aptar Pharma, Le Vaudreuil, France) were filled with 66 µL of this 23 cP fluorescein solution.

• Droplet size distribution was measured using a Spraytec® equipped with a 300-mm lens by actuating five nasal sprays manually at 4 cm from the laser. Spray pattern was determined by using a SprayVIEW® with automatic actuation of 5 devices at 70 mm/s at 5 cm from the laser. The spray angle was extrapolated from the spray pattern measurement.

• In vitro deposition of liquid nasal sprays was characterised in an adult male nasal cast (Aeronose™, courtesy of Aptar/DTF/Univ. of Tours) with chemical quantification on a spectrophotometer. [5,6]. One device per nostril was manually actuated into the nasal cast with a combination of different actuation positions: insertion depth of 10 mm and 15 mm; delivery angle (horizontal plane) of 30°, 45° and 60°; and a fixed angle from the centre wall of 5°, slightly tilted towards the septum. During the actuation, no flow was applied. The analysis was performed in triplicate per configuration.

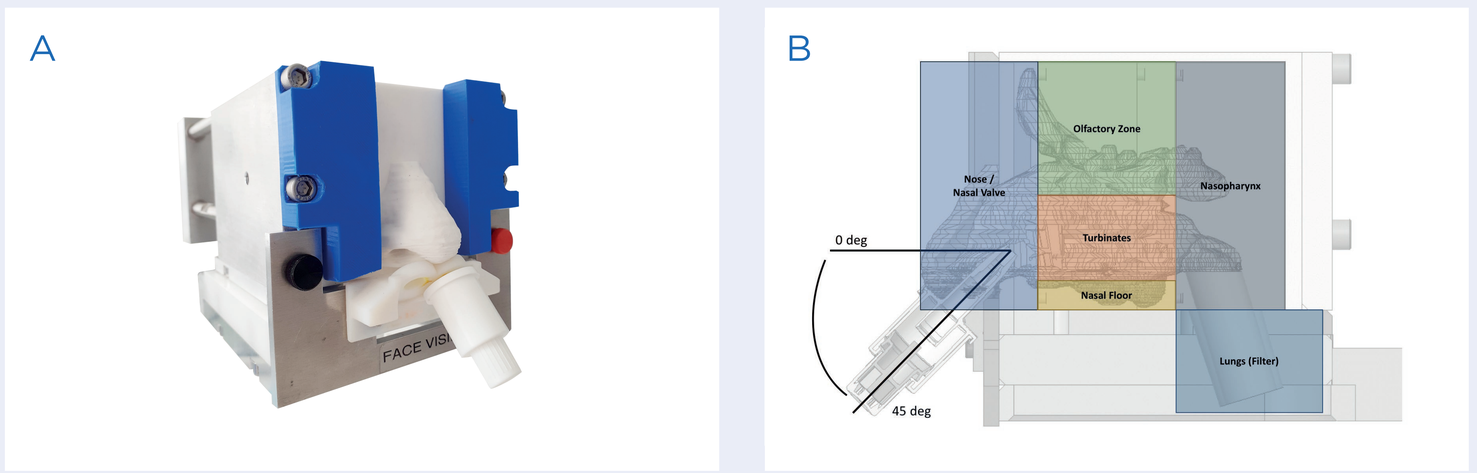

Figure 1 - (A) Experimental set-up for the nasal cast Aeronose™ in vitro deposition with a 3D printed jig that is fixed onto the nasal cast holder and controls the positioning of the device. (B) 3D representation with the blocks of the nasal cast and nasal regions which were separately quantified.

Results and Discussion

Spray Performance Characterization

• Due to the lack of a swirl chamber in the device and the higher viscosity of the formulation, a jet is visually observed and confirmed by laser diffraction measurements.

• This jet is also characterised by a small spray angle.

DSD d_{10} / µm	DSD d_{50} / µm	DSD d_{90} / µm	SP Area / mm²	Spray Angle / °
120 (15)	326 (26)	667 (27)	668 (61)	33 (1)

In Vitro Nasal Regional Deposition

• The deposition on the nasal floor, nasopharynx and filter (lungs) was negligible (below the limit of quantification).

• Both the angle and insertion depth had a significant impact on the deposition on the nose and turbinates (ANOVA, $p<0.01$).

• When increasing the horizontal angle from 30° to 60°, the deposition in the anterior area (nose and nasal valve) increased for both 10 mm and 15 mm insertion depth, while the deposition in the turbinates decreased.

• A higher deposition in the turbinates and lower deposition in the anterior region when increasing the insertion depth was observed.

• Concerning the olfactory area no significant difference was observed (ANOVA, $p=0.53$), which might be related to the lower deposition on this area for this specific formulation/device combination and the variability observed.

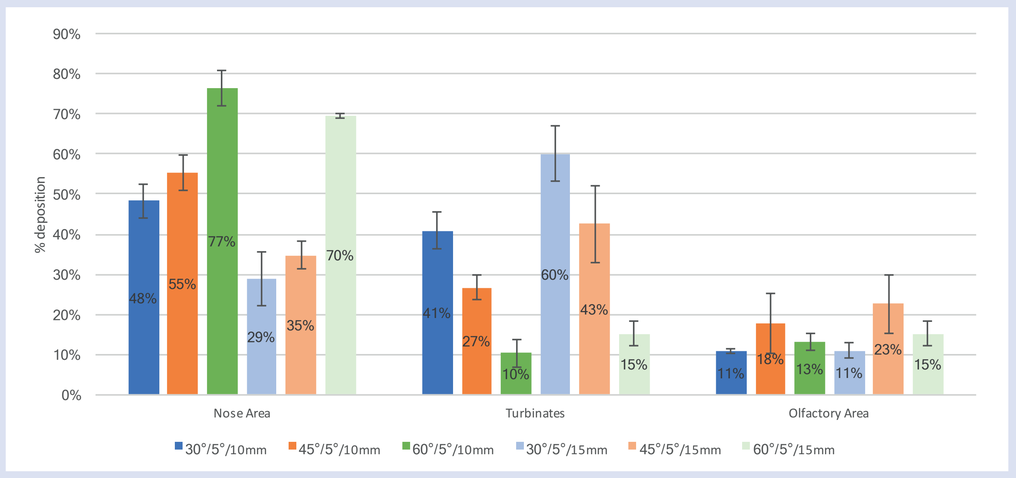

Figure 2 - Mean in vitro deposition from a nasal spray in a male nasal cast. Nasal floor, nasopharynx and filter (lungs) are not represented since their deposition was below the limit of quantification. Error bars show standard deviations (n = 3).

Conclusion

• For this liquid-filled unit dose powder device, lower angles (30 °) and higher insertion depths (15 mm) increased the posterior deposition (after the nose area).

• The highest deposition on the turbinates (systemic delivery [3]) was observed with 30 ° / 5 ° / 15 mm configuration. The highest deposition on the olfactory region (nose-to-brain) was observed with 45 ° / 5 ° / 15 mm configuration.

• Fixing the position of the device during the testing is a critical aspect to reduce the variability of the analysis and allow the accurate interpretation of these results during device and formulation screening activities.

• The adaptors used within this study could also be translated into a clinical environment, by using guides that limit the range positions that could be used by patients, and into a commercial environment, by designing specific features on the device to guide patients towards certain positions.

• Extending this study to different formulations and devices should be considered to optimize targeted nasal delivery.

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